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[Paolo Izzo](#) <sup>\*</sup>, [Luciano Izzo](#), Maurizio Cardi, [Andrea Polistena](#), [Daniele Crocetti](#), [Simone Sibio](#), Marcello Molle, [Claudia De Intinis](#), Sara Izzo

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*Observational study*

# Controlled Case Report on the Surgical Treatment of Recurrent Rectal Cancer: The Role of the Minimally Invasive Approach

Paolo Izzo <sup>1,\*</sup>, Luciano Izzo <sup>1</sup>, Maurizio Cardi <sup>1</sup>, Andrea Polistena <sup>1</sup>, Daniele Crocetti <sup>1</sup>,  
Simone Sibio <sup>1</sup>, Marcello Molle <sup>2</sup>, Claudia De Intinis <sup>1</sup> and Sara Izzo <sup>2</sup>

<sup>1</sup> Department of Surgery "Pietro Valdoni", Policlinico "Umberto I", Rome "Sapienza" University of Rome, 00128 Rome; p\_izzo@hotmail.it, deintinis.1891513@studenti.uniroma1.it, luciano.izzo@uniroma1.it, simone.sibio@uniroma1.it, andrea.polistena@uniroma1.it, maurizio.cardi@uniroma1.it, daniele.crocetti@uniroma1.it

<sup>2</sup> Department of Medical, Surgical, Neurologic, Metabolic and Ageing Sciences, Unit of Colorectal Surgery, University of Campania "Luigi Vanvitelli"; sa\_izzo@hotmail.it, marcello.molle@unicampania.it

\* Correspondence: luciano.izzo@uniroma1.it; Tel.: +39-3470103722

**Abstract:** (1) Background: The aim of this study is to investigate the diagnostic-therapeutic problem of pelvic recurrence of rectum cancer, highlighting current surgical standards and the possible role of the minimally invasive approach. This retrospective analysis of our surgical case study wishes to enter this debate while suggesting a possible line of action, based on the site of recurrence; (2) Methods: We examined, retrospectively, all the patients diagnosed, between 2008 and 2018, with cancer of the rectum at the "Pietro Valdoni" Department of Surgery and monitored their follow-up for 5 years. The sample consisted of 368 patients with rectal neoplasm, 136 females and 232 males, with an average age of 65.8 (ranging from 37 to 86); (3) Results: In 103 of the cases, the neoplasm was located in the upper rectum (28%), in 119 cases in the middle rectum (32.3%), in 102 cases in the lower rectum (27.7%), in 31 cases (8.4%) at the level of the right/sigma junction and in 13 cases it was not possible to define the site with certainty (3.5%); (4) Conclusions: The discussion remains open as to which approach is best at surgical level, whether laparoscopic, robotic or open-air. Our experience informs us that the most dangerous site remains on the anastomotic site.

**Keywords:** colorectal cancer; recurrent rectal cancer; laparoscopic surgery; robotic surgery; open-air surgery; controlled case report

## 1. Introduction

Carcinoma or cancer of the rectum is a malignant tumor is a form of cancer which contributes significantly to the spectrum of large intestine malignancies, accounting for approximately 30-35% of all cases within this category. Colorectal cancer, which encompasses both colon and rectal cancers, collectively constitutes around 10% of all diagnosed cancers. In Italy, this disease poses a substantial health burden, with an annual diagnosis rate of 12,000 individuals. It is estimated that 40 out of every 100,000 inhabitants are affected by rectal cancer, leading to an unfortunate yearly toll of 7,000 lives lost due to this disease<sup>1</sup>.

One notable aspect of colorectal cancer is that a significant proportion of patients, approximately 80%<sup>2</sup>, have tumors that are amenable to curative surgery (R0 resection). This implies that the tumor can be surgically removed without any residual cancerous tissue. However, despite the initial success of surgical intervention, a concerning phenomenon arises: approximately 40% of these patients experience disease relapse, often occurring within the first three years following surgery<sup>3</sup>. This relapse, known as local recurrence (L.R.), is characterized by the reappearance of malignant lesions at or near the site of the previous surgical procedure. Local recurrence after curative surgery of rectum cancer remains a clinical challenge today that requires a multidisciplinary approach and careful selection of patients suitable for surgery. The main risk factors associated with the onset of local recurrences include incomplete removal of the mesorectum, the presence of a resection margin

affected by the neoplasm (some authors report an 85% risk of local recurrence in these cases<sup>4</sup>), a disease-free margin of less than 2 mm<sup>5</sup>, tumor staging as B or C according to Dukes (with risks of 16.3% and 28.6%, respectively<sup>6</sup>), and onset in the lower third of the rectum<sup>7</sup>. Conversely, the use of surgical techniques such as Trans-Anal Endoscopic Microsurgery (TEM) and the presence of a disease-free margin of 6 mm or more have been associated with a lower risk of local recurrences<sup>8</sup>. Additionally, a higher risk of local recurrences has been observed in tumors with mucous histology<sup>9</sup>.

The pelvis is the primary site for local disease recurrence in rectal cancer: metastases at this level are mostly asymptomatic in many cases (50%) or may present with symptoms such as sacral and perineal pain or rectal bleeding<sup>10</sup> and they are typically discovered during imaging exams performed during follow-up<sup>11</sup>. Advances in TME surgery and the use of adjuvant and neoadjuvant therapies have reduced pelvic recurrence rates from 20-30% to 6-10% in recent population studies. Pelvic recurrences typically manifest within the first 5 years post-surgery, with 70% occurring in the first 2 years and 85% in the first 3 years. Surgical intervention with R0 resection, achievable in over 50% of cases, remains the sole potentially curative option, offering a 5-year survival rate of around 30%<sup>12</sup>. However, these surgeries can be complex, costly, and associated with significant morbidity<sup>13</sup>. Consequently, only a limited number of patients can benefit from them.

The aim of this study is to frame the diagnostic-therapeutic problem of pelvic recurrence of rectum cancer, highlighting the current surgical standards and the possible role of the minimally invasive approach. It is necessary to identify an approach to the treatment of recurrences that may be shared. Although the method of presentation cannot be identical in the different patients, it is necessary to identify whether the approach using the laparoscopic technique, the robotic technique, the open-sky technique and/or chemotherapy or radiotherapy is better and when and how these resources can be harmonized. This retrospective examination of our surgical case study wishes to enter the debate to propose a possible line of action to adopt according to the site of the recurrence.

## 2. Materials and Methods

We examined, retrospectively, all the patients diagnosed with cancer of the rectum between 2008 and 2018 treated at the "Pietro Valdoni" Department of Surgery and monitored their follow-up for 5 years. The sample consists of 368 patients with rectal neoplasm, 136 females and 232 males, with an average age of 65.8 (the range was 37-86 years). Subsequently, we conducted a literature search to compare the results of our experience with those of other authors.

## 3. Results

Among the 368 patients, 103 had cancer located in the upper rectum (28%), 119 in the middle rectum (32.3%), 102 in the lower rectum (27.7%), 31 at the right/sigma junction (8.4%), and 13 had unknown primary location (3.5%).

Curative surgery was feasible in 288 of these patients (78.26%), with 75 patients (20.4%) receiving neoadjuvant chemotherapy. Out of the 288 surgically treated rectal cancer patients, 31 (11%) experienced local recurrence. Additionally, 11 patients who had surgery for rectal cancer in another hospital were included in the study, making a total of 42 patients (with an average age of 65.8 years, ranging from 37 to 86). For the purposes of our study 35 out of the 42 patients who were free from distant metastases at the time of their first surgical operation were examined (Table 1).

**Table 1.** Layering of patients with local-regional recurrence. Legend: TEM (Trans-anal endoscopic microsurgery).

<b>Primary Cancer Therapy</b>		
<b>anterior resection</b>	21	60,0%
<b>Miles</b>	9	25,7%
<b>Hartmann</b>	4	11,4%
<b>TEM</b>	1	2,8%
<b>Radicality Primitive Cancer</b>		
<b>RO</b>	31	88,6%
<b>R1-R2</b>	4	11,4%
<b>Stage Primitive Cancer</b>		
<b>T1</b>	1	2,7%
<b>T2</b>	7	21,6%
<b>T3</b>	18	51,3%
<b>T4</b>	9	24,4%
<b>Dukes A</b>	2	5,7%
<b>Dukes B</b>	6	17,1%
<b>Dukes C</b>	27	77,2%
<b>Recurrences site</b>		
<b>Anastomotic</b>	13	37,1%
<b>Centre-pelvic</b>	11	31,4%
<b>Pre-sacral</b>	9	25,7%
<b>Perineal</b>	2	5,7%

In terms of primary tumor characteristics, 9 cases were T4 (25.7%), 18 cases were T3 (51.4%), 7 cases were T2 (20%), and 1 case was T1 (2.8%). The surgeries were performed using the open technique, with 21 patients undergoing anterior resection (60%), 9 patients undergoing perineal abdominal amputation according to Miles's technique (25.7%), 4 patients using Hartmann's surgical approach (11.4%), and 1 patient with TEM (Trans anal endoscopic microsurgery (2.8%). R0 resection was achieved in 31 cases (88.5%), while R1-R2 resection was done in 4 cases (11.5%). Neoadjuvant chemoradiation therapy was performed in 6 patients (17.1%), and 20 patients (57.1%) underwent adjuvant chemoradiation therapy.

Regarding the site of recurrence, 13 patients developed an anastomotic recurrence (37.1%), 12 had central-pelvic recurrences (31.4%), 9 had presacral recurrences (25.7%), and 2 had perineal recurrences (5.7%). Commonly infiltrated organs included the ureters, bladder, sacral and pelvic bones, with no documented involvement of the sciatic nerve or iliac vessels.

The disease-free survival interval between the diagnosis of recurrence and the previous surgery for the primary tumor was 13.4 months, ranging from 3 to 51 months. Abdominal pain was the primary symptom in 27 cases (77.1%), a palpable mass in 16 cases (45.7%), and an increase in tumor markers (CEA) was the initial sign in 12 patients (34.3%).

In 7 patients (20%), surgery was not feasible due to widespread lung and liver metastases (4 cases) or invasion of the sacral or pelvic bones. Palliative surgical therapy (ileum/colostomy) was performed in 5 cases (14.3%), while curative surgical therapy was carried out in the remaining 23 cases (65.7%) (Table 2).

**Table 2.** Treatment of recurrences.

<b>No therapy</b>	1	20%
<b>Palliative therapy</b>	5	14,3%
<b>Curative Surgery</b>	23	65,7%
<b>Re-resection</b>	10	
<b>nodule exeresis</b>	7	
<b>Intervention using the Miles's technique</b>	6	

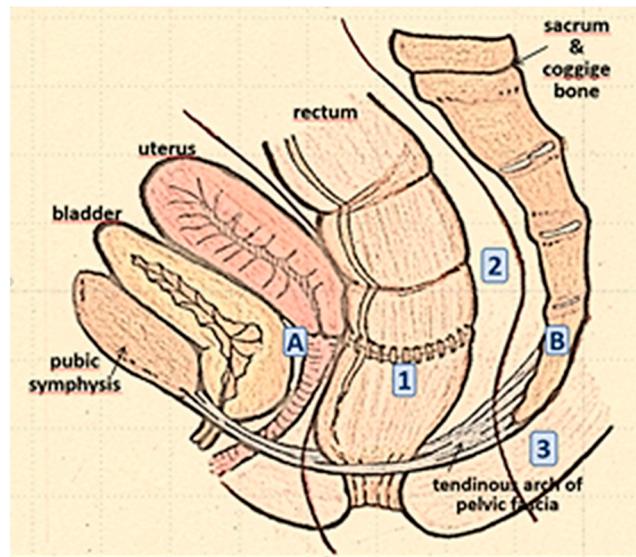
Out of these 23 patients, 7 underwent a new recto-colic resection (all of whom had previously undergone RAR), 10 underwent excision of the recurrence (5 of whom had a previous RAR, 4 had an abdominoperineal amputation, and 1 had a Hartmann intervention), and 6 had abdominoperineal amputation according to Miles (4 with a previous RAR, 1 with a Hartmann intervention, and 1 with a TEM). All procedures were performed using an open technique.

In 18 cases (64.2%), the resection was radical (R0), with a 2-year follow-up survival rate averaging 29.2 months, ranging from 9 to 85 months after the diagnosis of relapse. In the remaining cases (R1-R2), recurrence progression was observed in the following months, ranging from 2 to 13 months, with an average of 5 months.

Regarding integrated therapy, 23 patients (78.5%) underwent adjuvant chemotherapy and radiotherapy. Mortality was 7.1%, and morbidity was 42.8%, primarily due to anastomotic dehiscence (6 cases).

#### 4. Discussion

The management of pelvic metastases from colorectal cancer is complex. Even the classification of these metastases in the literature lacks unanimous consensus, with numerous classifications such as the Mayo Clinic classification<sup>12</sup> (based on the site of fixation and symptomatology), the Memorial Sloan Kettering classification<sup>13</sup> (Figure 1), and the Royal Marsden Hospital classification<sup>14</sup> (based on the degree of invasion of one or more of the seven pelvic compartments described in pre-operative MRI).



**Figure 1.** Anatomical sites of pelvic recurrence, sagittal views. A schematic figure suggested by the Memorial Sloan Kettering group: Axial, 1 Anastomotic, 2 Mesorectal, 3 Perineal, Anterior uterus/(prostate) A, Posterior, sacrum B.

The treatment of recurrence of rectal carcinoma is multimodal. The location and extent of the recurrence, together with an evaluation of previous treatment, should be considered when seeking guidance for the choice of the appropriate treatment strategy to adopt.

In many of the studies in literature, about 40-50% of patients with local recurrence are considered candidates for surgical exploration, though only 30-40% undergo R0 resection<sup>15</sup>.

Whatever the type of resection, it should always be performed by removing the recurrence and the affected adjacent organs or structures en-bloc. Careful patient selection is essential to exclude formal contraindications to surgery (Table3).

**Table 3.** Contraindications to surgical resection.

<ul style="list-style-type: none"> <li>- Stage IV disease</li> <li>- Extension of neoplasm beyond the large ischial foramen</li> <li>- Circumferential or extended neoplastic involvement of the lateral pelvic wall</li> <li>- Bilateral ureteral obstruction</li> <li>- Invasion of the sacral area over S2-S3</li> <li>- Invasion of the anterior pubic bone</li> <li>- Encasement (&gt;180°) of external iliac vessels</li> </ul>
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In the pre-Total Mesorectal Excision (TME) era, recurrences were often confined to the residual mesorectum or anastomotic sites. Today, recurrences can occur in any pelvic compartment, often necessitating extensive surgery.

The surgical approach typically involved a median navel-pubic laparotomy, preserving the lower epigastric vessels for potential use in a rectus abdominis muscle flaps. Several intraoperative scenarios could arise with this approach<sup>16</sup>:

- Non-fixed recurrence located at the anastomotic site or in the central compartment of the pelvis or in the perineal wound. In these cases, radical resection can be achieved by "limited" surgery: extensive local excision or rescue AAP or, if feasible, rectocolic resection.
- Anterior pelvic recurrence. If the genitourinary tract is involved, an en-bloc resection is recommended. A limited involvement of structures, such as the bladder dome or the posterior wall of the vagina, can be managed by partial excision with negative margins. Conversely, relapses with invasion of the bladder trigon or prostate in males and the uterine cervix in females usually require total pelvic exenteration. The mortality rate of this operation is still high (2-14%), as is the morbidity rate (33-75%)<sup>17</sup>.
- Lateral pelvic recurrence. These relapses have a worse prognosis because it is extremely difficult to obtain tumour-free resection margins (< 19%)<sup>18</sup>; sometimes these are impossible due to the involvement of larger vessels, the sciatic nerve, or pelvic bones.
- Dorsal recurrence. When the recurrence is localised in the dorsal compartment, an abdominal sacral resection can be performed. This operation is facilitated by a position of the patient in the ventral decubitus or "jack-knife" position. Although numerous studies in literature demonstrate the feasibility and safety of sacral resections below the S2/S3 junction, the risk/benefit ratio of such interventions is still under discussion, since they expose the patient to a high risk of neurological lesions (high sacrectomies) and uncontrollable venous bleeding (Table 4).

Moreover, it is not always easy to distinguish intraoperative bone infiltration from fibrous adhesions, as made evident by a recent series of 29 cases of recurrence reported by the Memorial-Sloan Kettering, where only 38% had real bone infiltration, while 68% regarded adhesions.

E) Extended recurrences. The indication for pelvic exenteration combined with secretory surgery is a dependent institution. To date, the highest number of cases of exenteration with sacrectomy by institution is that of Solomon and Milne of the Royal Prince Alfred Hospital in Sydney, with 100 patients operated, with an R0 resection rate of 72%, with an average survival-rate of 45 months and 5 years for 38%, complications in 74%, neurological complications (39%) in high sacrectomies<sup>17,19</sup>.

**Table 4.** Results of studies on abdominal-sacral resections.

Case	Study	Morbidity	Mortality	R0	Survival
Sagar <sup>20</sup>	40	60%	2.5%	50%	56% (3 years)
Ferenschild <sup>18</sup>	17	68%	0%	NA	45% (3 years)
Melton <sup>6</sup>					30% (5 years)
Moriya <sup>17</sup>	29	58%	3.4%	62%	63% (2 years)
Weber <sup>19</sup>	57	58%	4%	84%	20% (5 years)
Weber <sup>19</sup>	23	78%	0%	91%	54% (3 years)
					51% (3 years)

In recent years, laparoscopic and robotic approaches have become accepted methods for treating primary colorectal cancer. However, there is limited literature on follow-up studies regarding the safety and feasibility of laparoscopic surgery for the treatment of locoregional pelvic recurrence<sup>21,22</sup>(Table 5).

**Table 5.** Studies regarding laparoscopic surgery of recurrences from rectum cancer.

Author	Year	Cases	Site recurrences	Losses blood ml (average)	Time practitioners minutes (average)	Rate of resection R0	Postoperative Ratio mortality/morbidity
Lu <sup>23</sup>	2006	7	Central 6	200	211	100%	NR
			Presacral 1				
Kim <sup>24</sup>	2008	1	Central	50	185	100%	NR
Park <sup>25</sup>	2011	Lap:15 Open:26	Anastomotic, Ovary, Lymph nodes Lateral pelvis	NR	Lap: 150 Open: 259 p 0.059	Lap: 100%	Lap: 13.3% Open 57.7%
Nagasaki <sup>7</sup>	2014	Lap: 13 Open: 17	Central and Lymph nodes Lateral pelvis	Lap: 110 Open: 450 p 0.075	Lap: 381 Open: 241 p 0.024	Lap: 100%	Lap: 30.8% Open. 23.5%
Akiyoshi <sup>26</sup>	2015	9	Lymph nodes Lateral pelvis	130	381	100%	33.3%

The authors of these studies note that the minimally invasive approach offers the advantage of improved visibility, making dissection in a complex anatomical area like the pelvis, with altered anatomical planes, more precise. However, it's worth mentioning that these procedures often have longer operating times and demand a higher level of surgical expertise. Additionally, laparoscopic techniques tend to result in reduced blood loss, quicker restoration of intestinal function, and, from an oncological perspective, can achieve comparable rates of R0 resections<sup>23-25</sup>.

Ultimately, this approach should not be used for extended multi-visceral resections but limited to salvaging treatment of isolated central recurrences or of those closer to the lateral pelvic lymph nodes.

Pelvic recurrence of rectal cancer has significantly decreased in recent times thanks to the implementation of total mesorectal excision (TME) for rectal cancer and the integration of surgery with neoadjuvant chemoradiotherapy treatments. Most of these recurrences occur within 2 years of surgery, and without treatment, patients face an unfavorable prognosis with a substantial reduction in their quality of life, mainly due to severe pain. Non-surgical therapies like radiotherapy or chemoradiation therapy can provide some palliative relief, albeit with limited benefits and notable

side effects. Surgical treatment offers the best chance of survival when performed with curative intent. Achieving an R0 resection is now possible for up to 50% of patients, provided careful selection criteria are met<sup>26</sup>.

Limited surgery is a feasible option for isolated anastomotic and central peri-anastomotic recurrences, which have a relatively favorable prognosis with a 5-year survival rate of up to 65%. However, for ventral, dorsal, or lateral recurrences involving pelvic viscera or neighboring bone structures like the sacrum, a more extensive and en bloc resection is necessary. These highly complex and destructive operations should be performed in specialized high-volume centers by experienced multidisciplinary teams, including oncological surgeons, neurosurgeons, orthopedists, plastic surgeons, and other specialists. The goal of these procedures is to achieve an R0 resection, which can provide an average 5-year survival rate of up to 44%<sup>27</sup>.

In our case study, the rate of R0 resection was 65.7%, consistent with similar experiences reported in the literature (Table 2). The surgical interventions predominantly focused on favorable sites of recurrence, resulting in acceptable rates of mortality and morbidity.

While minimally invasive surgery offers advantages such as improved visualization and more precise dissection, it may not be suitable for extensive multivisceral resections that can only be achieved with open surgery. Multidisciplinary therapy is essential not only in managing primary rectal cancer but also in addressing its recurrence. Integrating radiotherapy, chemotherapy, and surgery increases resectability rates and yields promising outcomes in terms of recurrence percentages.management of cancer of the primary rectum but also to its recurrence.

## 5. Conclusions

Local recurrence of rectal cancer remains a significant complication, leading to poor survival and quality of life if left untreated. Advanced disease stage and non-radical surgery of the primary tumor are key risk factors. Early diagnosis is crucial, achievable through effective follow-up, especially during the initial 2-3 years post-surgery. Upon recurrence diagnosis, patients should receive comprehensive care from a multidisciplinary oncology team to determine the most suitable treatment. Rescue surgery is technically feasible and justifiable for specific patient groups. An aggressive multimodal approach can provide disease-free survival rates of up to 30% in carefully selected cases. Surgical resection demonstrates a more favorable cost-to-benefit ratio compared to non-surgical treatments. Refinements in diagnostic and staging methods, surgical techniques, chemoradiation therapy, and the availability of multidisciplinary teams hold promise for further improving surgical outcomes.

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