Article published online: 2022-12-22

Watch and Wait, Worth It?

Manoel Álvaro de Freitas Lins Neto[1] Luís Henrique Alves Salvador Filho[1]
Jorge Artur Peçanha de Miranda Coelho[2] João Otávio de Moraes Rolim[1]

[1] Coloproctology Service, Hospital Universitário Professor Alberto Antunes, Universidade Federal do Alagoas, Maceió, AL, Brazil
[2] Coloproctology Service, Faculty of Medicine, Universidade Federal do Alagoas, Maceió, AL, Brazil

Address for correspondence Manoel Álvaro de Freitas Lins Neto, Professor, Coloproctology Service of Professor Alberto Antunes University Hospital, Lourival Melo Mota Ave, Maceió, AL., 57072-900, Brazil (e-mail: manoel.alvaro@famed.ufal.br).

J Coloproctol 2022;42(4):308–314.

Abstract

Background The surgery with total mesorectal excision recommended by R. J. Heald in 1982 is the gold standard. Rectal cancer (RC) surgery has a morbidity rate ranging from 6 to 35%, and it can cause functional issues such as sexual, urinary, and bowel dysfunction in the long term. Neoadjuvant chemoradiotherapy (CRT) has been gaining ground in patients with lesions in the middle and lower rectum. The aim of the present study is to present the experience of a reference service in the treatment of RC.

Patients and Methods A retrospective study involving 53 patients diagnosed with RC between January 2017 and December 2019 with follow-up until December 2020. We examined tumor location, disease stage, digital rectal exam findings, carcinoembryonic antigen (CEA), therapeutic modality offered, and follow-up time.

Results A total of 32% of the patients were men and 68% were women, with a mean age of 60 years old. Location: upper rectum in 6 cases, middle rectum in 21 cases, and lower rectum in 26 cases with evolution from 9.8 to 13.5 months. The most frequent complaints were hematochezia and constipation. A total of 36 patients underwent neoadjuvant therapy: 11 complete clinical response (CCR) (30.5%), 20 (55.5%) partial clinical response (PCR), and no response in 5 patients (14%). The follow-up ranged from 12 to 48 months, with a mean of 30.5 months. A total of 25% of the patients had RC that went beyond the mesorectal fascia, and 22.64% had metastases in other parts of the body when they were diagnosed.

Conclusion Neoadjuvant radio and chemotherapy present themselves as an alternative in the treatment of rectal cancer. In 36 patients, 30.5% had a complete clinical response, 55.5% had a partial clinical response, and 14% had no response. It was worth doing the "Watch and Wait" (W&W) to sample. A definitive colostomy was avoided. However, it is necessary to expand the study to a larger follow-up and more patients. Additionally, it is necessary to implement a multicenter study.

Keywords
- rectum cancer
- neoadjuvant
- neoplasms
- colorectal surgery
- watch and wait

received
June 5, 2022
accepted after revision
September 15, 2022

DOI https://doi.org/10.1055/s-0042-1758206.
ISSN 2237-9363.

Thieme Revinter Publicações Ltda., Rua do Matoso 170, Rio de Janeiro, RJ, CEP 20270-135, Brazil

Introduction

The treatment of rectal cancer (RC) has evolved considerably over the last few decades. The gold standard is still surgery with total mesorectal excision recommended by R. J. Heald in 1982.[1] However, RC surgery carries a morbidity that varies between 06 and 35%, including bleeding, sepsis, and anastomotic dehiscence.[2] In addition, the surgery may be associated with long-term functional problems, for example sexual, urinary and defecation dysfunction, which can impact the quality of life of patients.[3]

Adoption of minimally invasive approaches through laparoscopy and robotics does not appear to significantly reduce the long-term morbidity associated with rectal cancer surgery.[3,4] Therefore, in the face of these problems, there has been a great interest in the behavior of organ preservation that involves techniques such as transanal endoscopic microsurgery (TEMS)[4] or observation and close clinical follow-up after the end of neoadjuvant therapy, "Watch and Wait" (W&W).[2]

Colorectal cancer (CRC) has high levels of incidence and mortality worldwide. In global terms, it is the third most commonly diagnosed neoplasm in men and the second in women.[5] In 2018, according to the World Health Organization (WHO), 1.8 million people were diagnosed and 861,000 died.[5] Specifically regarding RC, $\sim$ 43,340 patients are diagnosed annually in the United States of America.[6] It is the second most common neoplasm of the large intestine, just after colon cancer.[7] Despite the progressive decline in mortality since the 1990s, an average of 1.6 to 2% per year still, the rates are worrisome.[8] Genetical and environmental factors are related to the appearance of CRC.[5] History of the disease in a first degree relative and diagnosis of inflammatory bowel disease contribute to the development of this disease.[5]

Regarding RC, small lesions with superficial invasion are subject to local excision; however, most patients have lesions with deep invasion of the rectum, requiring transabdominal surgical procedures, such as low anterior resection of the rectum (LAR) or abdominoperineal resection of the rectum (APRR).[6] Tumors in the upper and middle rectum are usually managed with LAR, coloanal anastomosis, and anal sphincter preservation. Low rectal tumors, those that are $\leq$ 5 cm from the anal verge, are a great challenge in terms of local tumor control and anal sphincter preservation.[6] Abdominoperineal resection of the rectum is considered the standard surgery for tumors of the lower rectum, promoting excellent local control and survival. However, it implies a definitive colostomy, with a high incidence of urinary and sexual dysfunctions.[6] Sphincter-sparing procedures are approaches that try to dodge this situation, basically following two different paths. Superficial and small lesions confined to the wall of the rectum and subject to local resection; being able to offer local control and survival similar to APRR. For larger and more invasive lesions, neoadjuvant treatment (radiotherapy and chemotherapy) is indicated, with the possibility of promoting tumor regression and converting a programmed APRR into an anal sphincter-sparing procedure.[6]

Although not universally accepted, neoadjuvant approaches are generally indicated for T3/T4 stage patients, T1/T2 stage patients with positive lymph nodes during early staging, patients with lower rectum tumors in whom neoadjuvant chemoradiotherapy (CRT) may increase the capability of anal sphincter-sparing surgery, and for patients with RC that invades or approaches the mesorectal fascia, increasing the possibility of surgery with a disease-free circumferential margin.[9] Of the patients undergoing neoadjuvant CRT, a significant proportion (15 to 40%) had a complete pathological response (CPR), in which histopathological analysis of the surgical specimen does not show viable neoplastic cells. Patients who demonstrate CPR have an excellent prognosis, with local tumor recurrence rates close to zero, as well as 5-year survival rates $>$ 95%. It is then questioned whether, in the absence of neoplastic cells, the patient could be managed without a surgical procedure, sparing him the perioperative and long-term morbidity of an APRR.[10]

Developed by Habr-Gama et al., the nonoperative approach (W&W) for RC started to be offered to patients who, after neoadjuvant CRT, had a complete clinical response (CCR). In their classic work, Habr-Gama et al. defined CCR as failing to identify a viable tumor lesion on complete clinical examination (rectal examination and anoscopy), colonoscopy, radiological examinations, and serum carcinoembryonic antigen (CEA) levels; after neoadjuvant CRT. In that study, patients underwent investigation of clinical response between 8 and 10 weeks after the end of neoadjuvant CRT, those with residual tumor were referred for surgery, while patients with CCR were observed in the following 10 months. For those who maintained sustained CCR, the nonoperative approach was offered. In 5 years, overall survival and disease-free survival were 100 and 92%, respectively. Surgery remains the standard treatment for RC. However, W&W is considered safe and has high survival rates in a highly selected group of patients.[11]

The present paper presents the experience of the Coloproctology Service of the Hospital Universitário Professor Alberto Antunes in the management of patients diagnosed with RC, analyzing the clinical response of patients who underwent neoadjuvant CRT and follow-up through W&W observation, and analyzing the parameters for postoperative staging, mortality, postoperative complications, and patient follow-up.

Methods

Study Design and Setting

The present retrospective study was performed at the Hospital Universitário Professor Alberto Antunes (HUPAA, in the Portuguese acronym) of the Universidade Federal do Alagoas (UFAL, in the Portuguese acronym). Patients from January 2017 to December 2019 were included, with follow-up until December 2020. The coloproctology service of the HUPAA/UFAL opted for follow-up through the W&W in this manner: in the 1st and 2nd years of follow-up, digital rectal examination, sigmoidoscopy, and CEA measurement are performed quarterly; magnetic resonance imaging (MRI) of the pelvis every 6 months; and computed tomography (CT)

of the abdomen and chest annually; from the 3rd to the 5th year of follow-up, digital rectal examination, sigmoidoscopy, and CEA measurement are performed every 6 months. Annually, MRI of the pelvis and CT of the abdomen and chest; after the 5th year of follow-up, digital rectal examination, CEA measurement, colonoscopy, MRI of the pelvis, and CT of the abdomen and thorax are performed annually.

Data Source and Collection

Information was collected through electronic medical records. Fifty-three patients with rectal adenocarcinoma were selected. The variables investigated were gender, age, tumor location, disease stage, findings on digital rectal examination, CEA, therapeutic modality offered, and follow-up time.

The pretreatment evaluation consisted of a proctological examination, which included an anal inspection, a digital rectal examination, and anoscopy. Colonoscopy was performed in all patients, being complemented with virtual colonoscopy when the lesion prevented the device from progressing. Radiological staging was performed by MRI of the pelvis and CT of the upper abdomen and chest. Carcinoembryonic antigen (CEA) was requested for all patients.

For patients with RC, neoadjuvant CRT was recommended with the intention of treating in the lower and middle rectum with compatible staging T3 and T4 or T1/T2 with positive lymph node (N+). The neoadjuvant CRT offered to patients comprises chemotherapy with fluorouracil (5-FU) and leucovorin, concomitant with external radiotherapy in the pelvis with a dose of 45 Gy, in fractions of 1.8 Gy, followed by tumor boost up to 54 Gy. Tumor regression assessment was performed between 8 and 12 weeks after completion of neoadjuvant CRT and used the same clinical, endoscopic, and radiological tools as the pretreatment assessment. Patients who had a viable tumor after neoadjuvant CRT were referred to surgery; for patients who showed a complete response to neoadjuvant treatment, follow-up was performed using the W&W methodology. After neoadjuvant therapy, CCR is considered when there are no lesions on a digital rectal exam, an endoscopic exam, or an MRI scan of the pelvis. Partial clinical response was considered in subjects who had a reduction in tumor size ('downsizing') and staging ('downstaging') after neoadjuvant therapy. When the lesion grows back during patient follow-up, this is seen as a failure of the W&W.

Statistical Analysis

Data were revised, coded, and analyzed using the IBM SPSS Statistics for Windows version 25 (IBM Corp., Armonk, NY, USA). Numerical variables were expressed as mean and standard deviation (±SD). Qualitative data were expressed as frequency (f) and percentage (%).

Results

Of the 53 patients selected for the study (►**Table 1**), 17 (32%) were male and 36 (68%) were female. The patients were between 33 and 87 years old, with a mean age of 60 years (SD ± 14.2). Rectal cancer was identified through colonoscopy in the upper rectum in six cases, in the middle rectum in 21 cases, and in the lower rectum in 26 cases. A total of 46 lesions were identified by digital rectal examination (DRE). The lesions identified were classified as mobile (41.3%) or fixed (58.7%). A total of 32.1% of the cases corresponded to T4 staging, while 67.9% of the cases had a favorable prognosis (T1, T2, or T3 staging).

Table 1 Characteristics of the patients and of the tumors ($n = 53$)

Characteristics	Result*
Age (years old)	60.0 ± 14.2 (33–87)
Age ranges (years old)	
< 40	6 (11.3%)
40–50	7 (13.2%)
51–60	13 (24.5%)
61–70	11 (20.8%)
71–80	12 (22.6%)
> 80	4 (7.5%)
Sex	
Female	36 (67.9%)
Male	17 (32.1%)
Site of tumor	
Lower Rectum	26 (49.1%)
Middle Rectum	21 (39.6%)
Upper Rectum	6 (11.3%)
Lesion (DRE)	
Lower Rectum mobile	11 (23.9%)
Lower Rectum fixed	15 (32.6%)
Middle Rectum mobile	8 (17.4%)
Middle Rectum fixed	12 (26.1%)
Tumor staging	
T1	1 (1.9%)
T2	11 (20.8%)
T3	24 (45.3%)
T4	17 (32.1%)

Abbreviattion: DRE, digital rectal examination.
Note: *Described as "mean ± standard deviation (minimum - maximum)" or "frequency (percentage)".

The DRE identified (►**Table 2**) a fixed lesion corresponding to T4 staging in 10 cases (21.7%) and a mobile lesion in 4 cases (8.7%). In addition, the most frequent complaint was hematochezia (17 patients), followed by constipation (10 patients), with a mean time of evolution of 9.8 and 13.5 months, from the onset of symptoms to the moment of diagnosis. A total of 22.64% (12/53) of the patients had distant metastasis at diagnosis. All underwent CEA testing during staging. A total of 22 out of 53 (41.5%) had CEA > 5 mg/dL.

There were 36 patients (►**Table 3**) who underwent neoadjuvant therapy, 16 (44.4%) had a lesion in the middle

Table 2 Tumor lesion topography with digital rectal exam mobility and T staging (n = 46)

Lesion Topography / Digital Rectal Exam	T1	T2	T3	T4	Total
Lower Rectum fixed	1 (3.8%)	2 (7.7%)	6 (23.1%)	6 (23.1%)	15 (57.7%)
Lower Rectum mobile	0 (0.0%)	2 (7.7%)	6 (23.1%)	3 (11.5%)	11 (42.3%)
Total	1 (3.8%)	4 (15.4%)	12 (46.2%)	9 (34.6%)	26 (100%)
Topography + Digital Rectal Exam / Staging(T)	**T1**	**T2**	**T3**	**T4**	**Total**
Middle Rectum fixed	0 (0.0%)	2 (10.0%)	6 (30.0%)	4 (20.0%)	12 (60.0%)
Middle Rectum mobile	0 (0.0%)	2 (10.0%)	5 (25.0%)	1 (5.0%)	8 (40.0%)
Total	0 (0.0%)	4 (20.0%)	11 (55.0%)	5 (25.0%)	20 (100.0%)

Table 3 Relationship of response to neoadjuvant therapy and 'watch and wait' follow-up with tumor lesion topography

Lesion Topography	Complete response	Partial response	No response	Total
Middle Rectum	5 (13.8%)	8 (22.2%)	3 (8.3%)	16 (44.4%)
Lower Rectum	6 (16.7%)	12 (33.3%)	2 (5.5%)	20 (55.6%)
Total	11 (30.5%)	20 (55.5%)	5 (13.8%)	36 (100%)
CCR patients (followed-up with W&W):	**Failure (regrowth)**	**Sustained Remission**	**Total**	N/A
Middle Rectum	3 (27.3%)	2 (18.2%)	5 (45.5%)	N/A
Lower Rectum	5 (45.4%)	1 (9.1%)	6 (54.5%)	N/A
Total	8 (72.7%)	3 (27.3%)	11 (100%)	N/A
Patients who failed during W&W	**Earlier, failure**	**Later, failure**	**Total**	N/A
Middle Rectum	1 (12.5%)	2 (25.0%)	3 (37.5%)	N/A
Lower Rectum	3 (37.5%)	2 (25.0%)	5 (62.5%)	N/A
Total	4 (50.0%)	4 (50.0%)	8 (100%)	N/A

Abbreviattion: W&W, watch and wait. CCR, complete clinical response.
Note: N/A = Not applicable

rectum and 20 (55.6%) had a lesion in the lower rectum. For patients with lesions in the middle rectum, the reasons for not performing neoadjuvant treatment were: loss to follow-up ($n = 2$), palliative care ($n = 2$), and no formal indication for neoadjuvant therapy ($n = 1$ patient staged T2N0M0). For patients with lesions in the lower rectum, the reasons for not performing neoadjuvant treatment were: loss to follow-up ($n = 2$), palliative care ($n = 2$), and transfer to another service ($n = 2$). Of the 36 patients who underwent neoadjuvant therapy, 11 had CCR (30.5%). Partial clinical response was identified in 20 patients (55.5%) and no response in 5 (13.8%) patients.

The follow-up time of patients undergoing W&W ranged from 12 to 48 months, with a mean of 30.5 months. In this interval, W&W failure was identified in 8 (72.7%) patients. In 4 patients, the failure occurred in < 12 months (early failure) and in the other 4, in > 12 months (late failure). These patients were referred for a surgical procedure with curative intent. Four were submitted to LAR and four were submitted to APRR. Three patients had sustained remission.

Of the patients referred for surgery with curative intent, 17 underwent LAR, 13 underwent APRR, and 1 underwent total proctocolectomy. In all cases, tumor-free surgical margins were achieved. Between 0 and 37 lymph nodes were identified in the products of surgical resections (2 cases), totaling 373 resected lymph nodes, rendering an average of 12.03 lymph nodes per surgical piece.

One patient undergoing APRR had no neoplasm (yT0N0) as histopathological result of the surgical specimen. Seven patients underwent procedure for diversion of intestinal transit, with palliative purpose. Thus, 38 surgical procedures were performed. Mortality related to the surgical procedure was identified in 6 patients (15.8%), in whom the main causes were: pulmonary thromboembolism (3 cases), septic shock secondary to anastomotic dehiscence (2 cases) and pneumonia (1 case).

Discussion

The present study identified that patients diagnosed with RC showed some symptoms for ~ 1 year, until the moment of diagnosis (average of 10 months), in addition to the fact that a high percentage of patients had advanced disease at diagnosis. It is expected to diagnose ~ 10% of cases of RC with invasion beyond the mesorectal fascia[12]; however, the study casuistry shows just > 30% of diagnoses with this characteristic. Primary healthcare failed, as Abreu concludes in his study with 20% of patients with RC in his casuistry with distant metastasis at diagnosis.[13] Similarly, 22.64% (12/53) of the patients in the present study had distant metastasis at the time of diagnosis.

The highest number of diagnoses was in the female gender in comparison with the male gender (68 versus 32%), contrasting with global indexes, which point to a greater predominance of RC in the male gender, with an average incidence in this group of 13 cases/100,000 individuals per year.[13] Some factors may contribute to global variations in incidence rates, for example the different prevalence of risk factors for RC and different screening methods;[13] however, the lower number of diagnoses in the male gender may have a behavioral justification. In a study with $\sim$ 2,400 men representing the various regions of the country, it was observed that $\sim$ 37% of those $\leq$ 39 years old, and 20% of those $\geq$ 40 years old, admitted seeking medical advising only when feeling unwell. These numbers rise, respectively, to 47 and 28% for those who depend on the Unified Health System (SUS).[14]

In a systematic review, Nielsen et al. identified discrepancies between methodologies for classifying the topography of the lesions. There are studies that use MRI of the pelvis, others use colonoscopy, and some that are based on rigid proctoscopy. Another discrepancy factor is the distance from the anal verge which is considered rectum territory; some authors consider 15 and others 12 centimenters.[15] In the present study, the option was to classify the topography of the lesions based on colonoscopy and the relationship between the lesions and the Houston valves.

In general, studies on epidemiology, clinical presentation, and symptomatology tend to group colon tumors and rectal tumors together, describing them as CRC. Majumdar et al., in the article "How does colorectal cancer present? Symptoms, duration, and clues to location", observes that the mean duration of symptoms until diagnosis was 14 weeks, ranging from 1 week for obstructive symptoms to 27 weeks for patients who complained of weight loss. For the subgroup of patients with cancer distal to the splenic angle, the most common symptoms and their respective durations until diagnosis were: rectal bleeding (8 weeks), weight loss (27 weeks), and change in stool pattern, diarrhea or constipation, (9 weeks).[16] Our casuistry revealed that the most prevalent symptoms for patients with RC were rectal bleeding and constipation at 9.8 and 13.5 months, respectively. The overall average duration of symptoms until diagnosis was 10 months, longer when compared with study the study by Majumdar.

Carcinoembryonic antigen is a glycoprotein produced during fetal development, but that can be a sign of malignancy if produced after birth.[17] The analysis of CEA in CRC screening and diagnosis is still evolving. This marker has a sensitivity that varies between 46 and 59% and a specificity of 80%; however, CEA values can be influenced by other conditions and pathologies, such as: smoking, gastrointestinal infections, peptic ulcers, inflammatory bowel disease, pancreatitis, hypothyroidism, cirrhosis, biliary obstruction, in addition to thyroid, ovarian and lung neoplasms and melanoma.[17] Measurement of CEA is used to monitor the patient, constituting an important tool for controlling new lesions or metastasis after curative surgery.[17] A rigorous surveillance with periodic serum measurement of CEA for these patients has an impact on survival.[18] In the present study, the measurement of CEA was performed in the pretreatment assessment, in the postoperative follow-up and as a methodology for nonoperative management of the W&W. All patients underwent CEA testing during staging, 22/53 (41.5%) had CEA reagent ($>$ 5 mg/dL).

Digital rectal examination is an important diagnostic tool for patients with RC and should not be abandoned even with the evolution of imaging tests, especially MRI, currently the modality of choice for staging RC.[19] With MRI, it is possible to demonstrate the relationship of the tumor to adjacent structures and the bowel wall. The layers: muscularis mucosa, submucosa, and muscularis propria can be identified; as well as perirectal fat and the mesorectal fascia.[19] In a study published by Brown et al., which analyzed the effectiveness of preoperative staging based on digital rectal examination, endoanal ultrasound and MRI compared with histopathological analysis, it was concluded that digital rectal examination is able to correctly identify 71% (22/31) of RC patients with a good prognosis (staging T3 or lower), endoanal ultrasound correctly identified 45% (14/31), and MRI 100%.[20] We present in our casuistry the probability of rectal examination identifying a mobile lesion corresponding to an RC stage T1, T2 or T3 through MRI is 42.4% (14/33). In the Mercury study, when digital rectal examination showed a fixed lesion, correspondence with involvement of the circumferential margin was only 15% (10/68). T4 is 69.2% (9/13); in the present study, the probability of DRE identifying a fixed lesion corresponding to an RC T4 staging is 69.2% (9/13).

Neoadjuvant CRT for RC can provide important tumor downstaging and downsizing. In this context, tumors that show significant regression can be addressed with less invasive and sphincter-sparing strategies, or even without an immediate surgical procedure with strict outpatient follow-up.[2] However, the identification of these patients remains a challenge, even using radiological studies. Patients with an incomplete clinical response, with residual ulceration, may not have a viable tumor present; and the opposite is also valid; patients with apparent complete clinical response may have microscopic sites of tumor cells.[21] In a study published by Perez et al., with a series of 172 patients undergoing neoadjuvant CRT, a complete clinical response was observed in 60 cases, corresponding to a rate of 35%. The remaining 112 patients had a partial response (65%).[21] In the present study, of the 36 patients who underwent neoadjuvant therapy, 11 had a complete clinical response (30.5%); partial clinical response was identified in 20 patients (55.5%), and absence of response, an event that was not described in the casuistry of Perez et al., occurred in 5 patients (14%).

Chadi et al. compiled 11 studies, totaling 602 patients cataloged between 1990 and 2017, with a mean follow-up of 37.6 months. In the subgroup of 459 patients followed-up from 2008, when MRI staging became the gold standard, regrowth after 2 years of follow-up was 19% for patients with stage T1 and T2 tumors, 31% for T3, and 37% for T4.[22] In the present study, patients who were followed-up by W&W had a follow-up period that ranged from 12 to 48 months, with a

mean of 30.5 months. In this interval, tumor regrowth was identified in 8 of the 11 patients (72.7%). The study by Chadi et al. suggests that the high T staging criteria is an important factor for a higher risk of regrowth; as most of the patients in our study had an elevated T criteria at diagnosis; and associated with a restricted number of cases, bias was possibly established. It is important to consider that patients with more advanced T criteria (T3b-d/T4) may take longer to reach CCR than patients with T2/T3a.[23] By indicating a surgical approach to patients with excellent clinical response, even if partial, between 10 and 16 weeks by neoadjuvant CRT, one may be denying the possibility of nonoperative management with success potential.[23] Our paper documented a case with partial clinical response to neoadjuvant CRT and whose histopathological result was the absence of neoplasm (yT0N0).

In one patient of our casuistry with T2N0M0 staging, we chose not to perform neoadjuvant CRT, according to the thought that, specifically for cT2N0 patients, neoadjuvant CRT may not be necessary, since these patients have a low risk of local recurrence after a surgical procedure with total mesorectal excision. However, for patients in this group with indication for radical surgery, the benefits of neoadjuvant CRT in an attempt to avoid this type of approach are real. Gama et al. demonstrated that 80% of cT2N0 patients undergoing neoadjuvant CRT after achieving complete clinical response maintained sustained remission for a period of 5 years.[24] Such results demonstrate that knowledge improvement in the treatment of patients with RC through W&W is real, with good prospects. However, current data are from nonrandomized clinical trials and the W&W definition of complete clinical response and follow-up protocols are not standardized. We understand that the ideal management of patients with RC has not yet been fully elucidated. Thus, the approach must be individualized, considering the initial staging, expertise of the service and the desire of the patient.[25] To collect all available data to expand knowledge of the risks, benefits and oncological safety of organ preservation strategies in RC, the International Watch and Wait Databases (IWWD) was developed in 2014 by EURECCA and the Champalimaud Foundation. Studies established in this database can contribute to the formulation of an international consensus for staging, treatment, and follow-up protocols in RC.[26]

The detection of lymph node involvement is critical for the histopathological staging of RC, determining prognosis and identifying patients who may benefit from adjuvant therapy.[27] Langman et al., documented the surgical resection products of 244 patients; 173 underwent LAR and 71 APRR, making a total of 10,473 lymph nodes resected, a mean of 41 lymph nodes per surgical specimen (ranging from 31 to 52 lymph nodes); 344 of 10,473 (3.2%) were positive for neoplasm.[27] The casuistry presented by the Medical Residency Program in Coloproctology at the Santa Casa de Belo Horizonte for patients with CRC undergoing surgery reveals that the average number of ganglia found in the surgical specimens was 10.4 and a mortality of 16.2% for patients with CRC who underwent surgical procedures (12/74).[28] Our sample had a mean lymph node detection rate of 12.03 per surgical specimen (ranging from 0 to 37 lymph nodes); lymph node involvement by neoplasm was identified in 5.36% (20/373).

Surgery as a treatment for RC is associated with high rates of morbidity and mortality. The reasons that justify these rates remain under debate.[29] The main postoperative complications with death outcome documented in our study were: pulmonary thromboembolism (3 cases), septic shock secondary to anastomotic dehiscence (2 cases), and pneumonia (1 case), with a mortality of 15.78% (6/38). Smedh et al. documented 133 cases of RC patients undergoing surgical treatment in 4 hospitals in Sweden and identified a mortality rate of 8%.[29]

Diseases related to Disease-related Treatment Failure (DrTF), such as locoregional recurrence, distant metastasis, second primary tumor, or treatment-related death present themselves as a constant challenge in the management of patients with RC. Recent clinical trials have shown that local control for locally advanced RC has improved and a lower incidence of DrTF can be achieved with short-course neoadjuvant RT, followed by CT and total mesorectal excision, and conventional CRT afterwards. Additionally, higher rates of complete pathological response were demonstrated, which may reinforce the organ preservation approach.[30–32]

Conclusion

Of the 36 patients who underwent neoadjuvant therapy, partial clinical response was identified in 20 patients (55.5%) and no response in 5 patients (14%). The proportion of patients undergoing neoadjuvant CRT who presented CCR is consistent with the literature, reinforcing that it is worthwhile to persist in a behavior with adequate follow-up and organ preservation. The mortality related to the surgical procedure and the percentage of lymph node resection per surgical piece are equivalent to the literature consulted. It was worth doing the W&W to sample. A definitive colostomy was avoided. However, it is necessary to expand the study to a larger follow-up and more patients. Additionally, it is necessary to implement a multicenter study.

Conflict of Interests
The authors have no conflict of interests to declare.

References

1 Heald RJ, Husband EM, Ryall RD. The mesorectum in rectal cancer surgery–the clue to pelvic recurrence? Br J Surg 1982;69(10): 613–616. Doi: 10.1002/bjs.1800691019
2 Lai CL, Lai MJ, Wu CC, Jao SW, Hsiao CW. Rectal cancer with complete clinical response after neoadjuvant chemoradiotherapy, surgery, or "watch and wait". Int J Colorectal Dis 2016;31(02): 413–419. Doi: 10.1007/s00384-015- 2460-y
3 Shearer R, Gale M, Aly OE, Aly EH. Have early postoperative complications from laparoscopic rectal cancer surgery improved over the past 20 years? Colorectal Dis 2013;15(10):1211–1226. Doi: 10.1111/codi.12302
4 Scarpinata R, Aly EH. Does robotic rectal cancer surgery offer improved early postoperative outcomes? Dis Colon Rectum 2013; 56(02):253–262. Doi: 10.1097/DCR.0b013e3182694595

5 Macrae FA. Colorectal Cancer: Epidemiology, Risk Factors, and Protective Factors. Wolters Kluwer, UpToDate Waltham, MA: UpToDate Inc. (Accessed on January 07, 2021) https://www.uptodate.com

6 Willet CG. Neoadjuvant Chemoradiotherapy, Radiotherapy, and Chemotherapy for Rectal Adenocarcinoma P Ryan, UpToDate Waltham, MA.

7 Siegel R, Desantis C, Jemal A. Colorectal cancer statistics, 2014. CA Cancer J Clin 2014;64(02):104–117

8 Finlay AM. Clinical Presentation, Diagnosis, and Staging of Colorectal Cancer.

9 Ronald B. Pretreatment Local Staging Evaluation for Rectal Cancer. Wolters Kluwer, UpToDate Waltham, MA: UpToDate Inc. (Accessed on January 16, 2021.) https://www.uptodate.com

10 Smith JD, Ruby JA, Goodman KA, et al. Nonoperative management of rectal cancer with complete clinical response after neoadjuvant therapy. Ann Surg 2012;256(06):965–972. Doi: 10.1097/SLA.0b013e3182759f1c

11 Habr-Gama A, Perez RO, Nadalin W, et al. Operative versus nonoperative treatment for stage 0 distal rectal cancer following chemoradiation therapy: long-term results. Ann Surg 2004;240 (04):711–717, discussion 717–718 . Doi: 10.1097/01.sla.0000141194.27992.32

12 de Wilt JH, Vermaas M, Ferenschild FT, Verhoef C. Management of locally advanced primary and recurrent rectal cancer. Clin Colon Rectal Surg 2007;20(03):255–263. Doi: 10.1055/s-2007-984870

13 Miguel Henriques Abreu, Eduarda Matos, Fernando Castro Poças, Rosa Rocha and Jorge Pinto (October 10th 2011). Rectal Cancer Epidemiology, Rectal Cancer - A Multidisciplinary Approach to Management, Giulio Aniello Santoro, IntechOpen, DOI: 10.5772/25386

14 Figueiredo W. Assistência à saúde dos homens: um desafio para os serviços de atenção primária. Cien Saude Colet 2005; 10:105–109. Doi: 10.1590/S1413-81232005000100017

15 Nielsen LB, Wille-Jørgensen P. National and international guidelines for rectal cancer. Colorectal Dis 2014;16(11):854–865. Doi: 10.1111/codi.12678

16 Majumdar SR, Fletcher RH, Evans AT. How does colorectal cancer present? Symptoms, duration, and clues to location. Am J Gastroenterol 1999;94(10):3039–3045. Doi: 10.1016/s0002-9270(99)00510-9

17 LADEIRAS, Vera Maria Fernandes Bugalho et al. Análises sanguíneas na detecção de cancro. 2019. Dissertação de Mestrado.

18 Duffy MJ, van Dalen A, Haglund C, et al. Tumour markers in colorectal cancer: European Group on Tumour Markers (EGTM) guidelines for clinical use. Eur J Cancer 2007;43(09):1348–1360

19 Souza GD, Souza LRQ, Cuenca RM, Vilela VM, Santos BEM, Aguiar FS. Pre- and Postoperative Imaging Methods in Colorectal Cancer. Arq Bras Cir Dig 2018;31(02):e1371

20 Brown G, Davies S, Williams GT, et al. Effectiveness of preoperative staging in rectal cancer: digital rectal examination, endoluminal ultrasound or magnetic resonance imaging? Br J Cancer 2004;91(01):23–29

21 Perez RO, Habr-Gama A, Pereira GV, et al. Role of biopsies in patients with residual rectal cancer following neoadjuvant chemoradiation after downsizing: can they rule out persisting cancer? Colorectal Dis 2012;14(06):714–720

22 Chadi SA, Malcomson L, Ensor J, et al. Factors affecting local regrowth after watch and wait for patients with a clinical complete response following chemoradiotherapy in rectal cancer (InterCoRe consortium): an individual participant data meta-analysis. Lancet Gastroenterol Hepatol 2018;3(12):825–836. Doi: 10.1016/S2468-1253(18)30301–7

23 Habr-Gama A, São Julião GP, Fernandez LM, et al. Achieving a Complete Clinical Response After Neoadjuvant Chemoradiation That Does Not Require Surgical Resection: It May Take Longer Than You Think!. Dis Colon Rectum 2019;62(07):802–808. Doi: 10.1097/DCR.0000000000001338

24 Habr-Gama A, São Julião GP, Vailati BB, et al. Organ Preservation in cT2N0 Rectal Cancer After Neoadjuvant Chemoradiation Therapy: The Impact of Radiation Therapy Dose-escalation and Consolidation Chemotherapy. Ann Surg 2019;269(01):102–107. Doi: 10.1097/SLA.0000000000002447

25 On J, Aly EH. 'Watch and wait' in rectal cancer: summary of the current evidence. Int J Colorectal Dis 2018;33(09):1159–1168. Doi: 10.1007/s00384- 018–3116–5

26 Van de Valk M. The International Watch and Wait database (IWWD) for rectal cancer: an update. J Clin Oncol 2017;35(Suppl 4S) (abstr 521)

27 Langman G, Patel A, Bowley DM. Size and distribution of lymph nodes in rectal cancer resection specimens. Dis Colon Rectum 2015;58(04):406–414. Doi: 10.1097/DCR.0000000000000321

28 Oliveira RG, Faria FF, Junior ACBL, et al. Cirurgia no câncer colorretal – abordagem cirúrgica de 74 pacientes do SUS portadores de câncer colorretal em programa de pós-graduação lato sensu em coloproctologia. Rev bras Coloproct 2011;31(01): 44–57

29 Smedh K, Olsson L, Johansson H, Aberg C, Andersson M. Reduction of postoperative morbidity and mortality in patients with rectal cancer following the introduction of a colorectal unit. Br J Surg 2001;88(02):273–277. Doi: 10.1046/j.1365-2168.2001

30 Hospers G, Bahadoer RR, Dijkstra EA, et al. Short-course radiotherapy followed by chemotherapy before TME in locally advanced rectal cancer: The randomized RAPIDO trial. J Clin Oncol 2020;38(15, suppl)4006–4006

31 Garcia-Aguilar J, Patil S, Kim JK, Yuval JB, Thompson H, Verheij F, , & OPRA Consortium. Preliminary results of the organ preservation of rectal adenocarcinoma (OPRA) trial. J Clin Oncol 2020;38 (15 suppl)4008–4008. Doi: 10.1200/JCO.2020.38

32 Weiser MR. Total Neoadjuvant Therapy for Locally Advanced Rectal Cancer: PRODIGE 23 Trial. Ann Surg Oncol 2022;29(03): 1493–1495

