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Prognostic Factors of Locally Advanced Non Metastatic Rectal Cancer in Tunisia

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ABSTRACT

Introduction: Multimodal treatment based on radio chemotherapy and surgery has improved the local control rate of rectal cancer, but the metastatic relapse rate and overall survival remained stable. The purpose of our study was to analyze the prognostic factors of Overall survival (OS), event-free survival (EFS), locoregional recurrence-free (LFS) and metastasis-free survival (MFS). **Patients and methods:** It was a retrospective study of patients with locally advanced non-metastatic rectal cancer treated with radio-chemotherapy and surgery at Habib Bourguiba Sfax University Hospital from January 2009 to December 2017. **Results:** We collected 66 patients. 5-year OS and EFS were 53% and 60% respectively, and the 5-year DFS was 82%. DFS at 5 years was 73%. In multivariate analysis, the independent prognostic factors retained for OS were tumor perforation (p=0.02) peri-nervous sheathing (p=0.03) and presence of recurrence (p=0.04). Factors that significantly influenced EFS were delays in adjuvant CT beyond 8 weeks (p=0.009), presence of lymphovascular emboli (p=0.04), and invaded circumferential boundaries (p=0.03). An invaded circumferential margin was the only variable significantly influencing LFS survival in multivariate study (p = 0.02). The presence of peri-neural engorgement and lymph node invasion on anatomopathological examination of the surgical specimen were retained as pejorative prognostic factors of metastatic recurrence (p = 0.02). **Conclusion:** The prognosis of rectal cancers remains reserved. Accurate pre-treatment evaluation and optimization of neoadjuvant treatment according to disease prognostic factors could improve oncological outcomes.

Keywords: Radiotherapy, Chemotherapy, Rectal cancer

INTRODUCTION

Neoadjuvant chemoradiotherapy (n CRT) followed by radical surgery including total mesorectal excision (TME) is the recommended treatment in patients with locally advanced rectal cancer, that has showed its effectiveness to improve local control. Up to 10 to 30% of complete

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pathological response (pCR) is obtained after nCRT. Nevertheless, the distant progression and overall survival rates remain stable and the 5-year survival probability is about 70% [1,2].

The determination of prognostic factors allows improving the knowledge of the biology of the disease, the predictive factors of bad prognosis and directs the process of an intensification of the multimodal treatment. We carried out a study to identify the predictive factors associated with Overall survival (OS), event-free survival (EFS),locoregional recurrence-free (LFS) and metastasis-free survival (MFS).

PATIENTS AND METHODS

Patients with locally advanced non-metastatic rectal cancer who had concomitant radio chemotherapy (RT-CT) between January 2009 and December 2017 in Habib Bourguiba hospital in Sfax were evaluated retrospectively. All patients had digital rectal examination (DRE), rigid proctoscopy and abdominopelvic computed tomography. Pelvic magnetic resonance imaging was performed, when possible.

Preoperative 3D radiotherapy (RT) (45-50 Gy) combined with chemotherapy (CT) was indicated for tumors of the middle and lower rectum classified as T3-T4 and/or with lymph node involvement (N1-3). In case of surgical contraindication or refusal of the patient, a tumoricidal dose irradiation, with or without CT, was delivered.

For patients having primary surgery, in case of underestimation during the initial staging and in case of invaded margins, postoperative RT was proposed in association with CT in the presence of pejorative pathological factors: p T4, invaded lymph nodes, invaded circumferential margin and/or positive distal margin.

The modalities of rectal resection varied according to the location of the tumor, its possible extension to neighboring organs, the patient's terrain, and the state of the sphincter. All patients had total mesorectal excision surgery. The type of surgery was decided in the multidisciplinary consultation meeting before and after evaluation of the clinical response to preoperative treatment by clinical examination, proctoscopy and pelvic CT and/or MRI.

Age, sex, distance from the anal verge to the tumor, tumor mobility in DRE, clinical TNM staging (7th edition), tumor differentiation, macroscopic appearance of the tumor, endoscopic tumor size, circumferential extent, chemotherapy and radiotherapy regimens, interval between the radiotherapy and the surgery, CEA levels and data from the anatomopathological report of the surgical specimen are studied to identify prognostic factors on survival.

Statistical analyses were performed using "statistical package for the social science" (SPSS) version 21.0 for windows. Univariate analysis was performed using log-rank test and multivariate analyses were performed with the logistic regression test.

RESULTS

General data

We collected 66 patients. Median age was 55 years [34 to 83 years]. Sex-ratio was 0.8. Median time to consultation was 3 months [0-36 months]. DRE and proctoscopy concluded to distal rectum tumor in 35 cases (53%) and budding appearance in 86.4%. The most frequent histological type was Lieberkuhnian adenocarcinoma present in 58 patients (87.8%). Eight patients (12.2%) had mucinous colloid carcinoma. The tumors were well differentiated in 24 cases (36.4%).

Clinical and radiological exams concluded to T3 stage and node positive tumors in respectively 49 and 46 patients. Thus, 70% had clinical stage III and 22.7% had clinical stage II. Clinical Patients' characteristics are summarized in Table I.

Table I: Clinical Patients' characteristics.

Patients characteristics	N = 66 (%)
Age (years)	
Median	55
Range	34-83
Differentiation	
Well differentiated	24 (36.4%)
Poorly differentiated	8 (12.1%)
Moderately differentiated	25 (37.9%)
Not reported	9 (13.6%)
Tumor localization on DRE and proctoscopy	
Distal rectum	35 (53%)
Mid rectum	27 (40.9%)
High rectum	4 (6.1%)
T clinical stage	
T2	8 (12%)
T3	49 (74.2%)
T4	9 (13.6%)
Clinical lymph node involvement	
N+ 50 (71.4%)	46(70%)
N- 20 (28.6%)	20 (30%)
Clinical stage	
Stage I	5 (7.3%)
Stage II	15 (22.7%)
Stage III	46 (70 %)
Histological response	
pCR	6 (13.3%)
residual tumor	39 (89.7%)
Tumor response according to tumor regression system	
Dworak 0	5 (11%)
Dworak 1	20 (44.4%)
Dworak 2	12 (26.7%)
Dworak 3	2 (4.4%)
Dworak 4	6(13.3%)

Eleven patients had primary surgery followed by adjuvant RT-CT within a median of 14 weeks (7-24 weeks) and adjuvant chemotherapy. Four patients, considered as having high rectal tumor, were reclassified per operatively as middle rectal tumors. Eight patients had an anterior resection (AR) and 3 had abdomino perineal amputation. pT4 and pN+, R1 were noted in respectively 27.2% and 81.8% of cases.

Fifty-five patients had received neoadjuvant treatment followed by surgery in 45 patients. Surgery was anterior resection (RA) in 25 patients (55.5%), abdomino perineal amputation (PAA) in 18 patients (40%) and total Colo proctectomy in 2 patients (4.5%).

The median time from the end of CRT to surgery was 8 weeks. Four patients were lost to follow-up after RTCT and had reconsulted with recurrence of rectal bleeding at 7, 8, 24 and 25 months respectively, remaining non-metastatic and were therefore operated. 24 patients (53.3%) had a tumor classified as ypT3 with lymph node involvement in 15 patients. A complete histological response (pCR) was obtained in 6 patients (13.3%) and a tumor remnant (Dworak 0-3) was found in 39 patients (86.7%) (Table II). Twenty-nine patients had received adjuvant CT and four had received an additional dose of 20 Gy of RT postoperatively for invaded margins and. Treatment characteristics are summarized in Table III.

Table II: pathological characteristics.

After nCRT	N =45 (%)
Histological response	
pCR	6 (13.3%)
residual tumor	39 (86.7%)
Tumor response according to tumor regression system	
Dworak 0	5 (11%)
Dworak 1	20 (44.4%)
Dworak 2	12 (26.7%)
Dworak 3	2 (4.4%)
Dworak 4	6(13.3%)
Average lymph nodes removed	13 (3-31)
ypN+	15 (33.3%)
ypN1	9 (20%)
ypN2	6 (13.3%)
Upfront surgery	N=11 (%)
Average lymph nodes removed	9 (1-25)
pN+	10 (91%)
pN0	1(9.1%)
pN1	7 (63.6%)
pN2	3 (27.3%)

Table III: Survival based on anatomopathological factors.

Treatment characteristics	N (%)	
Type of concomitant chemotherapy		
Fufol	44	83%
LV5FU2	2	3.7%
5FU en continu	4	7.5%
Capécitabine	3	5.6%
Concomitant RT dose		
44 Gy	2	3.6%
50.4 Gy	2	3.6%
45 Gy	49	89%
64 Gy	2	3.6%
Type of Surgery		
AR	33	60%
APA	19	34%
CPT	3	6 %
Adjuvant CT		
Folfox	29	74%
LV5FU2	3	7.6%
XELOX	3	7.6%
Capécitabine	1	2.5%
Fufol	3	7.6%
Adjuvante RT dose		
45 Gy	7	46%
64 Gy	4	26%
20 Gy	4	26%

Table IV: Survival based on treatment-related factors.

	5 years OS		5 years LFS		5 years MFS		5 year EFS	
Delay of surgery : • ≤ 8 S • > 8 S	76% 58%	p = 0.08	93 % 76%	p=0.047	78% 79%	p = 0.8	73% 60%	p = 0.2
Surgery types • RA • AAP	67% 58 %	p = 0.2	80% 86%	p = 0.9	74% 79%	p = 0.6	60% 68%	p = 0.8
Delay of adjuvant CT • ≤ 8 S • > 8 S	64 % 43 %	p = 0.085	92% 71%	p=0.03	88% 53%	p=0.05	81% 38%	p =0.005
Duration of RT • ≤ 7 days • > 7 days	58% 44%	p = 0.1	79% 60%	p = 0.6	78% 72%	p = 0,6	61% 63%	p = 0.9

AR: anterior resection; AAP: abdominal-perineal amputation; OS: overall survival; RFS: recurrence-free survival; DFS: metastasis-free survival; EFS: event-free survival; w: weeks; CT: chemotherapy; RT: radiotherapy

Table V: Survival based on anatomopathological factors.

	5 year OS		5 year RFS		5 year MFS		5 year EFS	
Lymph nodes involvement: • pN0 • pN1 • pN2	80 % 46% 40%	**p = 0.02**	88% 67% 78%	p = 0.5	88% 66% 46%	p = 0.06	78% 44% 36%	**p = 0.04**
Extracapsular invasion • yes • no	34% 68 %	**p = 0.02**	100 81%	p = 0.3	36% 84%	**p=0.017**	35% 67%	p = 0.2
Parietal Invasion • pT1-pT2 • pT3-pT4	85% 54%	**p = 0.041**	84% 82%	p = 0.6	85% 73%	P = 0.4	71% 53%	P = 0.4
Stages: • I • II • III	100% 71% 45%	**p = 0.04**	100% 82% 97%	p = 0.5	100% 89% 61%	p = 0.06	100% 73% 48%	p = 0.1
Tumor perforation: • yes • no	34% 68%	**p = 0.023**	65% 85%	**p = 0.05**	76% 83%	p = 0.7	64% 54%	p = 0.2
Lymphovascular invasion: • yes • no	32% 67%	p = 0.05	81% 85%	p = 0.7	45% 85%	**p = 0.02**	40% 69%	**p = 0.01**
Peri-nervous sheathing • yes • no	34% 80%	**p = 0.001**	79% 85%	p = 0.2	54% 89%	**p = 0.01**	43% 75%	p = 0.07
Colloïde Component: • yes • no	52% 53%	p = 0.6	84% 80%	P = 0.3	71% 79%	p = 0.7	57% 66%	p = 0.3
Tumor differentiation: • little • Moderately • Well différencieted	22% 50% 76%	**p = 0.046**	37% 93% 80%	p = 0.07	100% 75% 81%	p = 0,7	37% 70% 64%	p = 0,6
Tumoral growth • ≤ 5cm • > 5cm	78% 38%	**p = 0.008**	86% 64%	**p = 0.03**	81% 87%	p = 0 ,7	70% 56%	p = 0,1
Tumoral regression • Yes (Dworak : 1-4) • no (Dworak : 0)	71% 33%	**p = 0.02**	86% 66%	**p = 0.03**	100% 80%	p = 0,4	67% 66%	p = 0,2
Dworak Score • 0 • 1-2 • 3-4	33,3 % 65 % 75 %	p = 0.06	66% 85% 86%	p = 0.09	100% 79% 72 %	p = 0,7	66% 68% 63%	p = 0,5
Complète Response: • yes • No	66,7% 62%	p = 1	71% 80%	p = 0,8	82% 62%	p = 0,2	63% 50%	p = 0,3
Circonférentiel Margin • safe • invaded	70% 41%	p = 0.09	89% 63%	**p = 0.01**	82% 70%	p = 0,2	73% 43%	**p = 0,007**

OS: overall survival; RFS: recurrence-free survival; MFS: metastasis-free survival; EFS: event-free survival

The average number of lymph nodes removed was 13 [3-31] for patients operated on immediately and 9 [1-25] for patients operated on after neoadjuvant treatment. The number of lymph nodes removed was greater than 12 in 25 cases (44%). (Table II)

Distal resection margins were not invaded in all patients. The average margin was 3 cm. Four patients had a margin of less than 1 cm. They had undergone PAA. The mean clearance was 4.1 mm. It was less than 1 mm in 16 cases (28.4%) of which four were operated firstly, indicating adjuvant radio chemotherapy. Vascular and lymphatic emboli were found in 15 cases (26.8%) and peri-neural sheathing in 25 cases (44.6%), indicating adjuvant chemotherapy.

Overall survival (OS) and event-free survival (EFS) at 5 years were 53% and 60% respectively, and locoregional recurrence-free (LFS) and metastasis-free survival (MFS) at 5 years were 82% and 73% respectively.

Prognostic Factors

Univariate analysis:

Treatment-related factors: (Table IV)

-For patients who had neoadjuvant RT-CT; OS, LFS, MFS, and EFS at 5 years were 55.7%, 85%,78%, and 61%, respectively, versus 34%,72%,64%, and 46% for patients who had adjuvant treatment. However, the difference was not significant.

-Neoadjuvant treatment-surgery delays: For surgery within 8 weeks or less, the 5-year LFS was 93% versus 76% if this time was exceeded (p = 0.04).

-Surgery was a statically significant factor in 5-year OS (61% versus 10% for non-operated patients).

-The 5-year OS was 65.8% for patients who had adjuvant CT versus 75% for patients who did not have adjuvant CT (p=0.09).

-For patients who started their adjuvant CT within 8 weeks or less, the 5-year LFS, MFS, and EFS were 88%, 92% and 81%, respectively, versus 53%, 71% and 38% for those who started later (p<0.05)

-OS for patients with a RT interruption of 7 days or more was 44% versus 58% (p = 0.1)

Anatomopathological factors (table V):

-The number of invaded nodes influenced significantly OS and EFS.

-The presence of extracapsular invasion was predictive of metastatic relapse and decline of OS.

-Extensive parietal invasion significantly influenced 5-year OS (85% for pT1and pT2 versus 54% for pT3 and pT4 (p = 0.041).

-Tumor perforation was a predictive factor of local relapse, 5-year LFS was 65% versus 85%. It affected also OS significantly.

-The presence of vascular and/or lymphatic emboli was predictive of metastatic relapse with a 5-year DFS of 45% versus 85% (p = 0.02). It also significantly impacted OS and EFS.

-The presence of peri-nervous sheathing was a predictor of metastatic relapse. It also significantly impacted OS with an OS of 34% versus 80% (p = 0.001).

-The presence of colloid component did not affect survival.

-Tumor differentiation significantly impacted OS (p = 0.04).

-A tumor size of 5cm or more significantly influenced the OS of patients with a 5-year OS of 38% versus 78% for others (p = 0.008).

-Statistical analysis showed no significant association between the degree of histological response and survivals. OS and LFS were better for patients with a partial histological response (Dworak = 1-2) than for patients with a near-complete and complete tumor response (Dworak = 3-4)

The group with tumor regression regardless of grade showed a gain in OS compared to the group with no therapeutic effect on histology: 71% at 5 years versus 33% at 5 years (p: 0.02). RFS was significantly lower in the group with no therapeutic response.

-Invaded circumferential resection margins significantly impacted LFS (p = 0.01) and EFS (p = 0.007).

Multivariate Analysis

In multivariate analysis, the independent prognostic factors retained for OS were tumor perforation (p=0.02) peri-nervous sheathing (p=0.03) and presence of recurrence (p=0.04).

Factors that significantly influenced EFS were delays in adjuvant CT beyond 8 weeks (p=0.009), presence of lymphovascular emboli (p=0.04), and invaded circumferential boundaries (p=0.03).

An invaded circumferential margin was the only variable significantly influencing LFS survival in multivariate study (p = 0.02).

The presence of peri-neural engorgement and lymph node invasion on anatomopathological examination of the surgical specimen were retained as pejorative prognostic factors of metastatic recurrence (p = 0.02).

DISCUSSION

Therapeutic management of rectal cancer has seen many

advances during this century. The oncological results are in clear progression thanks to the development of neoadjuvant treatments, to the notion of total excision of the mesorectum and to the techniques of sphincter conservation. It remains, however, inherent to several factors related to the patient, the tumor or the surgeon. The determination of these factors is essential in order to optimize the management and monitoring of this cancer.

Our study, although retrospective, analyzed most of the prognostic factors discussed in the literature.

Patient-related Factors

For some authors, age >70 years was found to be an independent factor affecting OS [3]. In the Algerian study, no significant difference was found in terms of survival depending on the age group. The analysis is similar for our series.

Tumor-related Factors

Lower rectal cancers are considered to have a poorer prognosis than middle rectal cancers [5]. Some studies have shown that the trend to develop lung metastases was significantly higher for low rectal tumor location. However, with neoadjuvant therapy and improved surgical techniques the prognosis of lower rectal tumors is currently comparable to that of the middle rectum [6]. Our study did not show any significant difference in survival whatever the site of the tumor.

Preoperative T-staging of rectal cancer by imaging is a complicated. Most errors in staging with imaging occur in distinguishing between T2 and limited T3 lesions with over classification caused by the desmoplastic reaction surrounding the lesions [8].

The prognostic heterogeneity of T3 disease has been recognized: patients whose cancer was less than 5 mm beyond the muscularis propria had a significantly better prognosis than those whose cancer was more than 5 mm beyond the muscularis propria in terms of local recurrence and cancer-related survival. MRI has good accuracy for the T category and should be considered for preoperative staging of rectal cancer [9].

The presence of positive lymph node is also a strong prognostic indicator. The likelihood of lymph node metastasis increases with the T-stage of the tumor. Lateral lymph node dissemination occurs in 10-25% of patients with rectal cancer, more often in lower rectal cancers thus increasing the risk of systemic dissemination. However, only 65% of mesorectal nodes found on histopathology can be visualized by MRI [10]. The present studies investigating prognostic factors of rectal cancers used the pathological node classification [11]. Our study did not demonstrate a prognostic correlation between initial parietal infiltration on imaging and lymph node involvement. Indeed, only 50% of our patients had an abdominopelvic MRI and the T3 subgroup classification was not present in the reports.

Treatment-related Factors

Regarding surgical treatment, two prospective studies had compared the different surgical techniques namely PAA and RA for tumors of the middle and lower rectum [12]. These studies did not find any significant difference in OS. This was also found in our study.

Since the Lyon R90-01 trial, 6 to 8 weeks was retained as the appropriate time interval between RT-CT and surgery since it may lead to better pathological tumor regression. But it does not influence the local recurrence rate and does not improve survival [13].

Recently, a growing number of studies have suggested that a longer time interval to surgery is associated with an improved pCR rate [14]. A meta-analysis demonstrated that the pCR rate is significantly higher in patients operated on after an interval ≥ 8 weeks compared to those operated on at < 8 weeks with no significant increase in postoperative complication rates and no effect on survivals or sphincter preservation rates [15]. THE GRECCAR-6 trial compared 2-time intervals between neoadjuvant therapy and surgery (less or greater than 11 weeks). The group >11 weeks had more morbidities (44.5% vs. 32% p: 0.04) and more medical complications (32.8% vs. 19.2% p: 0.013) as well as a worse quality of mesorectal resection but with no significant difference on pCR rate nor on 3-year OS or DFS [16]. Currently, several other recent retrospective studies have shown that a time interval of 10 weeks is the time frame for a better pCR rate [17].

French recommendations keep the optimal time for surgery between 6 and 8 weeks after long CT RT [18]. In our series, this delay was respected in 60% of the cases. Thirty percent were operated on within 8 weeks. In univariate analysis, patients operated on in more than 8 weeks had a higher rate of local recurrence.

In the literature, there is limited evidence that adjuvant CT improves distant relapse rates and OS in rectal cancer [19]. Analysis of the impact of adjuvant CT in our patients showed comparable MFS rates between patients who required CT and those who did not as well as OS (20), Our study also demonstrated in multivariate analysis that this delay was an important factor influencing OS (p = 0.03).

Anatomopathological Factors

The number of positive lymph nodes does not correlate

with the severity of the disease [21]. The American Joint Committee on Cancer recommends that at least 12 lymph nodes must be dissected during rectal cancer surgery for accurate staging. However, the number of lymph nodes dissected is often less after preoperative RT-CT due to lymph node atrophy, fibrosis, and lymphocyte depletion. Currently, the lymph node ratio (LNR = the number of invaded nodes over the number of nodes removed) is considered a better predictor that can replace the original staging system (TNM) of colorectal cancer [22]. In the study by Peng et al, patients were divided into three groups according to NRL (less than 0.14, NRL between 0.14 and 0.49 and NRL greater than 0.5-1). The 5-year disease-free survival rates of patients in the three groups were 72.57%, 58.54%, and 34.75% ($p < 10-3$), respectively. The 5-year OS rates were 72.19%, 61.92%, and 38.47% ($p<0.002$), respectively [23]. Our study showed that the degree of lymph node involvement according to the TNM classification correlates well with short DFS and OS, but it should be noted that only 25 of our patients (44.6%) had more than 12 nodes removed [24].

The presence of extra capsular invasion (ECI) was closely related to poor survival. It is a predictive factor for recurrence even after adjuvant RT-CT and CT. A meta-analysis and review of 13 studies showed a significant increase in mortality and recurrence in node-positive patients with ECI and increase in the risk of recurrence [25].

The degree of pT parietal invasion was a prognostic factor identified at an American consensus conference. Vessels are present in the third layer of the rectal wall which corresponds to a T3 stage of parietal infiltration according to the TNM classification. Any invasion of the rectal wall beyond this stage is associated with vascular invasion and thus a higher risk of dissemination and recurrence. Our study and another Tunisian publication showed that pT3-pT4 stages were associated with an increased risk of recurrence [26]. It was associated with a decrease in OS for our patients. Accidental perforation remains a significant risk factor for local recurrence. In a Swedish study, for operated TNM stage I-III rectal cancer (R0), the local recurrence rate increased after perforation. The 5-year OS rate was lower after perforation [27]. The perforated tumor rate in our study was 19%, which correlated with a lower OS and RFS.

Lymphovascular invasion (LVI) is defined as tumor invasion into vascular and lymphatic structures. This factor is well known for the metastatic spread of cancer, which also negatively impacts overall survival. Patients with LVI have unfavorable disease-free survival and 3-year OS. Our results are consistent with the literature. EFS, OS and MFS were lower than in patients without LVI. The presence of LVI was an independent factor for EFS [28].

A meta-analysis showed that EPN was independently associated with poor survival in 7 of the 11 studies [29]. Two Korean studies including patients treated with preoperative CRT followed by TME surgery showed that EPN was a worse prognostic factor compared to ILV for DFS and OS [30]. Low tumor differentiation is one of the best known predictors of local and distant recurrence and incomplete response to neoadjuvant RT-CT. Karakgounis et al demonstrated that it is an independent factor of the decrease in EFS in multivariate analysis but this difference is noted in the short term becoming negligible after 3 years [31].

The influence of tumor size on survival is controversial in [4]. In our study, a tumor size of 5 cm or more significantly influenced OS of patients with OS and 5-year DFS.

Indeed, a better overall survival rate and disease-free survival were noted in patients with a complete histological response versus those with a tumor residue [32]. In the study of Jaffel H, there was a positive impact of tumor regression on histology [26].

Our study also demonstrated in case of tumor regression, a gain in OS and EFS compared to no therapeutic effect on histology. In addition, there was a decrease in OS for patients with a partial response (Dworak score = 1-2) compared to those with a near-complete and complete histological response (Dworak score = 3-4) without significant differences. This may be due to the low number of patients with a Dworak score of 3 and 4. CRM is the main predictor of local recurrence and survival in rectal cancer. The threshold used to define an invasive CRM remains controversial: The Surveillance, Epidemiology (SEER) program conducted a large study of 10181 patients and demonstrated that a margin ≤ 1 mm is the predictive threshold for local recurrence and specific mortality. This threshold is the same as that defined by the European and French societies [33]. The local recurrence rate in our study was 37% versus 11% in case of negative CRM ($p = 0.01$) with a significantly lower event-free survival (73% versus 43%). Neoadjuvant RT-CT and MCT reduced the incidence of positive CRM to 10%. The rate of positive CRM found in our study was 28.5% higher than the rate described in the literature. This can be explained by the number of patients operated on immediately and the limited access to pelvic MRI (only 50% of patients had a preoperative pelvic MRI. Indeed, 9% of the patients operated on immediately had an invaded CRM [8]. The relative risk of local recurrence for sub-millimeter CRM on MRI was 3.5 in this study. Therefore, surgeons should strive for healthy CRM. In preoperative MRI or pathology, reports the CRM should be accurately measured in millimeters, rather than simply described as “invaded” or “clear.” This may provide better treatment and follow-up strategies for clinicians.

CONCLUSION

According to our study, 5-year OS and EFS were 53% and 60% respectively, and the 5-year DFS was 82%. DFS at 5 years was 73%. Factors associated with decreased OS were tumor perforation, presence of peri-neural sheathing and presence of recurrence. Those that significantly influenced event-free survival were delays in adjuvant CT beyond 8 weeks, presence of lymph vascular emboli, and invaded circumferential boundaries. The presence of peri-neural sheathing and positive adenopathy on pathological examination of the surgical specimen were associated with metastatic relapse. An invaded circumferential margin was a source of loco-regional relapse. The prognosis of rectal cancers remains reserved. Accurate pre-treatment evaluation and optimization of neoadjuvant treatment according to disease prognostic factors could improve oncological outcomes.

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