



Quality assessment of rectal cancer surgery: How are we doing?

Evaluation de la qualité de résection dans la chirurgie du cancer du rectum : Où en sommes-nous?

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ABSTRACT

Introduction: Surgery remains a cornerstone in the treatment of rectal cancer. Optimal surgical resection implies respect for carcinologic principles. The best way to evaluate a good quality of resection requires certainly an exhaustive evaluation of the surgical specimen by the surgeon and the pathologist.

Aim: To assess the quality of resected rectal cancers.

Methods: This study included patients operated on for rectal malignant epithelial tumors, between January 1st, 2015 and December 31st, 2020, in the general surgery department B at Charles Nicolle's Hospital in Tunis. Data relevant to the pathologic examination were recorded. We performed a descriptive study and an analytic bivariate study comparing the two groups «number of lymph nodes harvested less than 12» versus «number of lymph nodes harvested higher than or equal to 12».

Results: Neoadjuvant therapy was performed in 39 patients (79%). Anterior resection (AR) was performed in 43 patients (43%) and abdominoperineal resection (APR) was performed in 11 patients (20%). There were no invaded margins. The mean distal surgical margin was 3 ± 1.4 cm. Mesorectum was complete in 38 surgical specimens (70%). The median number of lymph nodes harvested was 14. Resection was considered R0 in 47 patients (87%). In bivariate analysis, there was no difference between the «number of harvested lymph nodes <12» and the «number of harvested lymph nodes ≥ 12 » groups for the variables: laparotomy, laparoscopic approach, conversion to laparotomy and chemoradiotherapy.

Conclusion: Quality of surgical resection of rectal cancer in our department was in accordance with recommendations.

Key words: Rectal neoplasms, surgery, proctectomy, pathology, quality improvement, lymphnode excision, chemoradiotherapy.

RÉSUMÉ

Introduction: La chirurgie reste la pierre angulaire du traitement du cancer du rectum. Une résection chirurgicale optimale implique le respect des principes carcinologiques. La meilleure façon d'évaluer la qualité de la résection nécessite certainement une évaluation exhaustive de la pièce opératoire par le chirurgien et le pathologiste. Cette étude a pour but d'évaluer la qualité des résections de cancers du rectum.

Méthodes: Cette étude a inclus les patients opérés pour des tumeurs épithéliales malignes rectales, entre le 1er janvier 2015 et le 31 décembre 2020, dans le service de chirurgie générale B à l'hôpital Charles Nicolle de Tunis. Les données relatives à l'examen anatomopathologique ont été enregistrées. Nous avons réalisé une étude descriptive et une étude analytique bivariée comparant les deux groupes « nombre de ganglions prélevés inférieur à 12 » versus « nombre de ganglions prélevés supérieur ou égal à 12 ».

Résultats: Un traitement néoadjuvant a été réalisé chez 39 patients (79%). Une résection antérieure a été réalisée chez 43 patients (43 %) et une amputation abdominopérinéale a été réalisée chez 11 patients (20 %). Il n'y a pas eu de marges envahies. La marge chirurgicale distale moyenne était de $3 \pm 1,4$ cm. Le mésorectum était complet dans 38 pièces opératoires (70 %). Le nombre médian de ganglions lymphatiques prélevés était de 14. La résection a été considérée comme R0 chez 47 patients (87 %). En analyse bivariée, il n'y avait pas de différence entre les groupes «nombre de ganglions lymphatiques prélevés <12» et «nombre de ganglions lymphatiques prélevés ≥ 12 » pour les variables suivantes : laparotomie, coelioscopie, conversion en laparotomie et radiochimiothérapie.

Conclusion: La qualité de la résection chirurgicale du cancer du rectum dans notre service était conforme aux recommandations.

Mots-clés: tumeurs rectales, chirurgie, proctectomie, anatomo-pathologie, amélioration de la qualité, curage ganglionnaire, radio chimiothérapie.

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INTRODUCTION

Colorectal cancer is the third most common cancer location and the second most common cause of cancer mortality in the world (1). Rectal cancer is still a public health problem in Tunisia. Its management is multidisciplinary (2). In the past, the prognosis of rectal cancer was poor, due to the risk of local recurrence because of an incomplete excision (3). Extra fascial excision of the mesorectum developed by Heald in the 1980s has now become a surgical standard (4,5). This technique has allowed us to define the quality of surgical excision of rectal cancers as a prognostic factor for local recurrence and survival. Therefore, collaboration between surgeons and pathologists is necessary to offer the best treatment to the patient. The pathologists play a key role in modern multidisciplinary management. They have the opportunity and responsibility to give feedback to the whole team of surgeons, radiologists and oncologists on the quality of their specimen management. The pathology report of the surgical excision specimens must provide some information based on histopronostic criteria that are essential for an optimal therapeutic management of the patient.

In order to ease this task, several healthcare organizations (the French National Cancer Institute (INCa) and the French Society of Pathology (SFP)) have published recommendations concerning the minimum pathology data to be provided with the aim of standardizing the pathologist's response (6). This standardization is intended to provide optimal therapeutic management for the patient. Few studies have analyzed the implementation of these recommendations in current practice (2,6).

The aim of our work was to assess the implementation of the recommendations concerning pathology data and to evaluate the quality of carcinologic surgical resection of rectal cancer in our surgical department.

METHODS

This was a longitudinal descriptive retrospective study, collecting consecutive patients operated on for a rectal tumor between January 01, 2015 and December 31, 2020 at the general surgery department «B» at Charles Nicolle Hospital in Tunis. We included all patients who had an elective radical surgery for a rectal malignant epithelial tumor. These patients were included regardless of gender, age, previous prescription or not of neoadjuvant therapy and regardless of the surgical approach. We did not include patients who had undergone surgery for epithelial dysplasia or non-epithelial malignant tumors. We had no exclusion criteria. Since the aim of our work was to judge the quality of surgical resection, we chose the number of harvested lymph nodes as the primary endpoint. Secondary endpoints were the integrity of the mesorectum according to the Quirke classification (7), and the proximal and distal resection margins. The patients were operated by median or laparoscopic approach. The surgical procedure consisted in an anterior resection (AR) or an abdominoperineal resection (APR) after multidisciplinary consultation. Specimens were fixed immediately with formalin and sent the next day for pathologic study. We recorded the following data concerning the tumor intraoperatively, the macroscopic and pathologic examination: tumor location relating to the peritoneal reflection line, size, proximal and distal resection margins, tumor perforation, invasion of adjacent organs, extent of resection to invaded adjacent structures, integrity of the mesorectum according to Quirke's classification

(7), histological type, circumferential resection margin (CRM), invasion of the resection margins, tumor extension according to the TNM 2017 classification (8), lymph node harvest superior or inferior to 12 lymph nodes, invasion of the distal doughnut, Crohn's like reaction, tumor budding, number of intraepithelial lymphocytes, tumor regression grade (TRG) according to the Mandard classification (9).

Statistics:

The data collected were analyzed using SPSS 25.0® software. We performed a descriptive study and a bivariate study comparing the two groups «number of lymph nodes harvested less than 12» versus «number of lymph nodes harvested higher than or equal to 12». Continuous variables were expressed as mean \pm standard deviation (SD). For variables that demonstrated high level of skewness, data were presented as median with extreme values. Categorical variables were expressed by their numbers and percentages. They were compared using the Pearson X2 test or Fisher exact test where appropriate. Statistical significance was set at a level of $p \leq 0.05$.

RESULTS

We enrolled 24 men (44%) and 30 women (56%), with a sex ratio of 0.8. The tumor location was the upper rectum in 15 patients (27%), middle rectum in 23 patients (43%) and lower rectum in 16 patients (30%). Neoadjuvant treatment was performed in 39 patients (72%). It consisted in neoadjuvant radio-chemotherapy in 37 patients, radiotherapy only in one patient and chemotherapy only in one patient. The most common procedure was AR in 43 patients (80%). APR was performed in 11 patients (20%). Laparotomy was done in 43 patients (79%). The laparoscopic approach was performed in 11 patients (21%). Conversion to laparotomy was performed in five patients. An extended monobloc resection was performed in four patients (7%): a left annexectomy in one patient, a colectomy in one patient, an extended resection to the bladder peritoneum in one patient and to the bladder peritoneum and appendix in one patient. Tumor perforation was observed intraoperatively in six patients (11%). The mean distal surgical margin estimated intraoperatively was 3 ± 1.4 cm [extreme values: 1 and 6 cm]. In the upper rectum, the mean distal surgical margin was 4.4 ± 1.2 cm [extreme values: 2 and 6 cm]. In the middle rectum, it was 2.6 ± 1.2 cm [extreme values: 1 and 5 cm]. In the lower rectum, the mean surgical distal margin was 2.3 ± 0.8 cm [extreme values: 1 and 4 cm]. In pathologic study, the mesorectum was complete in 38 surgical specimens (70%), nearly complete in six surgical specimens (11%) and incomplete in ten surgical specimens (19%). Pathologic examination concluded to a subperitoneal localization of the lower edge of the tumor in 33 patients (61%) and to a supraperitoneal localization in 21 patients (39%). The mean length of the surgical specimen was 27.7 cm \pm 10.5 cm [extreme values: 6 and 67 cm]. The median tumor height was 3.8 cm [extreme values: 0.7 and 9 cm]. The median tumor width was 3 cm [extreme values: 0.5 and 10 cm]. The median tumor thickness was 1.7 cm [extreme values: 0.4 and 7 cm]. The median distance of the upper edge of the tumor from the proximal section was 21.3 cm \pm 10.2 cm [extreme values: 3.5 and 60 cm]. The median distance of the lower edge of the tumor from the distal section was 2.6 cm [extreme values: 0.2 cm and 8.5 cm]. In the upper rectum, this distance was 3 cm [extreme values: 0.3 and 8.5 cm].

In the middle rectum, it was 2 cm [extreme values: 0.5 and 4 cm]. In the lower rectum, it was 2.5 cm [extreme values: 0.2 and 4.5 cm]. For APRs, the length of the anal canal was specified in 4 patients (36%). The mean length was 2.3 cm ± 0.5 cm. The circumferential extent of the tumor was specified in 52 surgical specimens (96%): this extent was respectively one quarter in 12 specimens (22%), one half in ten specimens (19%), three quarters in 12 specimens (22%), total in 18 specimens (33%). CRM was mentioned in 42 patients (78%). The CRM was 7 mm [extreme values: 0 and 25 mm]. The different macroscopic aspects, budding, infiltrating, planar, ulcerating-budding, ulcerated, were respectively found in 23 (42%), 40 (74%), 2 (4%), 14 (26%) and 30 (55%) tumors, knowing that a tumor could have several macroscopic aspects at the same time. Only one abscess in the mesorectum (2%) was found on all specimens. Tumor infiltration of adjacent organs was noted in three patients (5%). The infiltrated structures were the bladder, the small intestine and the vagina. There was no associated inflammatory colitis or diffuse polyposis. On three surgical specimens (5%), polyps adjacent to the tumor were noted: one sessile polyp and two pedunculated polyps. The median number of polyps was 2.3 [extreme values: 1 and 5 polyps]. The median size of the polyps was 9 mm [extreme values: 5 and 13 mm]. All examined distal doughnuts were free of carcinomatous proliferation. Only one distal doughnut (2%) was the site of an adenoma. The mean length of distal doughnut was specified in 22 patients among 40 distal doughnuts referred for pathologic examination. This length was 1.7 ± 0.6 cm [extreme values: 0.3 and 3 cm]. The majority histological type was moderately differentiated adenocarcinoma (ADK) in 25 patients (46%). The other histological types are shown in (Table 1).

Table 1. Patients according tumor histological type

| Tumor histological type | Well differentiated ADK | Moderately differentiated ADK | Poorly differentiated ADK | Signet ring cell carcinoma | Mucinous ADK |
|-------------------------|-------------------------|-------------------------------|---------------------------|----------------------------|--------------|
| N=54 | 23 | 25 | 3 | 1 | 2 |
| % | 42 | 46 | 6 | 2 | 4 |

The tumors were classified as T3 in 36 patients (66%) according to the TNM classification (Table 2).

Table 2. Patients according to TNM stage

| | N=54 | % |
|----------|------|-----|
| T | | |
| T0 | 2 | 4% |
| T1 | 2 | 4% |
| T2 | 11 | 20% |
| T3 | 36 | 66% |
| T4 | 3 | 6% |
| T4a | 2 | 4% |
| T4b | 1 | 2% |
| N | | |
| Nx | 1 | 2% |
| N0 | 32 | 60% |
| N1 | 15 | 28% |
| N2 | 6 | 10% |
| M | | |
| Mx | 1 | 2% |
| M0 | 51 | 94% |
| M1 | 2 | 4% |

Mucus component was observed in 14 patients (26%). No lymph node metastasis was observed in 32 patients (60%). The median number of lymph nodes harvested was 14 [extreme values: 0 and 45 lymph nodes].

A number of nodes harvested ≥ 12 was observed in 32 patients (59%). The median number of metastatic lymph nodes was 1 [extreme values: 0 to 23 lymph nodes]. Six patients (11%) had lymph node yield from the inferior mesenteric artery that were referred separately. They were metastatic in only one patient. No peritoneal metastasis was observed. Lymphatic emboli were identified in 11 patients (20%). Extramural venous invasion was identified in 11 patients (20%). Peri-nervous emboli were identified in 16 patients (30%). Crohn's like reaction was studied in 30 patients (55%). It was present in eight patients (26%). Tumor budding was studied in 34 patients (63%). It was present in 16 patients (47%). Among the 39 patients who had neoadjuvant treatment, TRG was studied on 32 specimens (82%) (Table 3).

Table 3. Patients according to TRG

| | TRG 1 | TRG 2 | TRG 3 | TRG 4 | TRG 5 |
|------|-------|-------|-------|-------|-------|
| N=54 | 1 | 3 | 5 | 13 | 10 |
| % | 3% | 9% | 16% | 41% | 31% |

The resection was considered R0 in 47 patients (87%) and R1 in seven patients (13%). All R1 resections were in relation with an invaded circumferential margin (≤ 1 mm). In bivariate analysis, there was no difference between the «number of harvested lymph nodes < 12» and the «number of harvested lymph nodes ≥ 12» groups for the variables: laparotomy, laparoscopic approach, conversion to laparotomy and chemoradiotherapy (Table 4).

Table 4. Patients according to harvested lymph nodes (cut-off fixed at 12)

| | Harvested lymph nodes < 12 N=22 (%) | Harvested lymph nodes ≥ 12 N=32 (%) | Total N=54 | p-value |
|---------------------------------|--|--|---------------|---------|
| Laparotomy | | | | |
| Yes | 16 (73) | 27 (84) | 43 | 0,240 |
| No | 6 (27) | 5 (16) | 11 | |
| Laparoscopy | | | | |
| Yes | 3 (14) | 3 (9) | 6 | 0,472 |
| No | 19 (86) | 29 (91) | 48 | |
| Conversion to laparotomy | | | | |
| Yes | 3 (14) | 2 (6) | 5 | 0,324 |
| No | 19 (86) | 30 (94) | 49 | |
| Chemoradiotherapy | | | | |
| Yes | 18 (82) | 19 (59) | 37 | 0,081 |
| No | 4 (18) | 13 (41) | 17 | |

The figures in parenthesis are percentages across the columns

DISCUSSION

We collected 54 pathology reports from patients operated on for rectal cancers. Forty-three patients underwent AR and 11 patients underwent APR. The median number of lymph nodes harvested was 14. A number of lymph nodes harvested higher than or equal to 12 was observed in 32 patients (59%). Mesorectum was complete in 70% of patients, nearly complete in 11% and incomplete in 19% with tumor perforation in 11%. Improvement in the quality of the report in recent years has been noted, especially with regard to factors that influence the quality of surgical resection, such as mesorectum integrity or the tumor regression grade (TRG), which did not exist in previous reports: two criteria for good evaluation of the quality of surgical resection and therefore which have a carcinologic impact. This suggests that it is probably due to the use of synoptic reports (89.5% in 2015 compared with 49% in 2007-2008 in a national study in New Zealand) (10).

The strengths of this work were firstly to standardize the pathology report, responding consequently to international standards, and secondly to insist on criteria that influence the correct surgical removal of rectal cancers (11). Indeed, this excision is evaluated according to specific criteria like number of lymph nodes harvested, CRM, the quality of excision of the mesorectum and the distal margin.

«The American Joint Committee on Cancer and the American College of Pathologists recommend examination of at least 12 lymph nodes to identify stage II rectal cancer (12). Pathologic assessment of lymph node status in patients with non-metastatic rectal cancer is essential and is the most important element in the evaluation of patients with non-metastatic rectal cancer (13). In a multicentric study in 2005, the median number of lymph nodes was estimated to be eight (14). The number of lymph nodes harvested depends on the surgeon, the pathologist, the tumor and whether or not neoadjuvant therapy (pre-operative chemoradiotherapy) has been given (15-16). Indeed, in our study, 82 % of patients who had lymph nodes harvested less than 12, had neoadjuvant radio-chemotherapy. However, only 59% of patients with had lymph nodes harvested more than 12, had radio-chemotherapy. Even there is no statistically significant difference between the two groups, these results highlight the impact of chemoradiotherapy in reducing the number of lymph nodes which is similar to data in the literature (17). Tumors involved the lower rectum has been observed in 16 patients (30%), APR was performed in 11 patients. In fact, APR has been considered the procedure of choice for locally advanced lower rectal tumors. The R1 resection (probable microscopic residue) is assessed by the distal and circumferential margins (18) The distal margin is defined as the distance from the lower edge of the tumor to the resection level (18). The mean distal surgical margin was 4.4 cm in the upper rectum, it was 2.6 cm in the middle rectum and 2.3 in the lower rectum. These results are comparable to the literature except for the lower rectum (18), since even patients who had APR for lower rectal cancers were included. The circumferential margin (CRM) is defined as the shortest distance in millimeters from the outer edge of the tumor or an adenopathy, tumor nodule or vascular embolus and the fascia recti. Out of the 54 patients, the median circumferential margin was 7 mm, and 87% of these patients had a circumferential margin larger than 1mm and 13% had a circumferential margin less than or equal to 1mm. In a Swedish single-center study of 448 patients made in 2015, 7% of patients had a CRM of 1mm or less. This did not correlate with survival or risk of local recurrence. The two most likely causes of a positive CRM were advanced tumor stage or technical malfunction.

The quality of mesorectal resection is also a marker of surgical resection quality (19). Our series showed a complete mesorectum in 70% of patients. Several studies have focused on the quality of mesorectal resection. Indeed, complete resection of the mesorectum has been reported in series with a rate varying from 23 to 57% (20,21,22,23). This enhances the quality of resection in our series insisting on the extra fascial resection described by Heald and consequently reducing the locoregional recurrence rate significantly.

The weak points of our series were the absence of some quality factors of good surgical resection such as the TRG and the quality of resection of the mesorectum, which existed in 32 out of 39 possible pathologic reports. CRM was not specified in 12 patients (22%). Mesorectal resection was incomplete in 18 patients, indicating technical malfunction or probably advanced tumor stage.

CONCLUSION

Quality assessment of rectal cancer resection through this study has allowed us to overview and to state how we are doing currently. Our results seem to be consistent with international standards for total mesorectal excision technique, adequate lymph node yield, appropriate rate of free distal and circumferential resection margins. We need to highlight that the pathologic reports were not all exhaustive. We believe that structured and standardized pathology reporting could be the best way to improve quality assessment and so carcinologic prognostic of operated rectal cancers.

Abbreviations:

AR: Anterior resection

APR: Abdominoperineal resection

SD: Standard deviation

INCa: French national cancer institute

SFP: French society of pathology

CRM: circumferential resection margin

TRG: Tumor regression grade

ADK: Adenocarcinoma

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