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# Rectal cancer survival in a Brazilian Cancer Reference Unit

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ABSTRACT

Colorectal cancer is one of the most common malign tumors in men and women all over the world. In spite of prevention advances in the last few years, worldwide incidence remains significant, about one million per year.

*Objectives:* Evaluate rectal cancer survival in patients diagnosed and surgically treated at the Cancer Reference Unit at Rio Grande do Norte State, Brazil.

*Methods:* Observational retrospective study composed by 135 patients assisted from 2007 to 2014 at Doctor Luiz Antonio Hospital, Natal, Brazil. Data were collected from the patient records revision and survival rates were calculated and analyzed by non-parametric Kaplan–Meier and Wilcoxon tests, respectively. All patients were submitted to surgical treatment, chemotherapy and/or radiotherapy.

*Results:* Overall survival was 62% in seven years, while disease-free survival in one, three and five years was 91.7%, 75.5% and 72.1%, respectively.

*Conclusion:* Overall survival and disease-free survival remained enhanced until the end of the study, suggesting that the treatment protocols used in the institution have shown to be effective.



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## Sobrevivência de câncer colorretal em uma Unidade de Referência do Câncer

*Palavras-chave:*
Câncer colorretal
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Sobrevida

RESUMO

O câncer colorretal é um dos tumores malignos mais comuns em homens e mulheres em todo o mundo. Apesar das melhorias na prevenção nos últimos anos, a incidência global ainda é expressiva, cerca de um milhão por ano.

*Objetivos:* Avaliar a sobrevida do câncer de reto nos pacientes diagnosticados e tratados cirurgicamente na Unidade de Referência do Câncer no Rio Grande do Norte, Brasil.

*Métodos:* Estudo observacional retrospectivo composto por 135 pacientes, compreendido no período de 2007 a 2014 no Hospital Dr. Luiz Antônio, Natal, Brasil. Os dados foram coletados através da revisão de prontuários e as sobrevidas foram calculadas e comparadas utilizando, respectivamente, os métodos não-paramétricos de Kaplan-Meier e teste de Wilcoxon. Todos os pacientes foram submetidos a tratamento cirúrgico, quimioterápico e radioterápico.

*Resultados:* A sobrevida global foi de 62% em sete anos, sendo a sobrevida livre de doença em um, três e cinco anos de 91,7%, 75,5% e 72,1%, respectivamente.

*Conclusão:* As sobrevidas global e livre da doença são elevadas até o encerramento do estudo, o que demonstra que os protocolos de tratamento utilizados na instituição têm se mostrado eficazes.



## Introduction

Colorectal cancer (CRC) is one of the most common malign tumors in men and women all over the world. In spite of prevention advances in the last few years, worldwide incidence remains significant (about one million per year). CRC causes more than 500,000 deaths per year and is the third most common cause of cancer-related deaths.

Brazilian National Cancer Institute estimates for the year of 2016 in Brazil 16,660 newly diagnosed cases of CRC in men and 17,620 in women.[1]

In a regional perspective, excluding non-melanoma skin tumors, CRC is the fourth most frequent in men in Brazilian Northeast (5.34/100,000). For women, is the third most frequent in the same region (8.77/100,000).[2]

Many risk factors could contribute to the development of CRC, as age, diet, genetic factors, predisposing medical conditions and tobacco. People with more than 40 years age have higher risk of CRC development, with a peak at 65 years age in United States. Occidental diet is also a risk factor for colon carcinoma due to the high intake of animal fat, exposing colonic mucosa to high levels of carcinogenic compounds. The occidental low fiber diet also promotes a low intestinal transit, which increases the exposition time to colonic carcinogenic.[3] Considering genetic factors, susceptibility to CRC includes well-defined hereditary syndromes, as Lynch Syndrome often called hereditary non polyposis colorectal cancer (HNPCC) and Familial Adenomatous Polyposis (FAP). Therefore, it is recommended that family history of CRC patients should be consulted and considered in a risk evaluation.[4]

A variety of surgical approaches, considering location and extension of the disease, are used to treat the rectal cancer primary lesions. These methods include local procedures, as polypectomy, transanal excision and transanal endoscopic microsurgery, and more invasive procedures involving transabdominal resection (for example, low anterior resection, proctectomy with total mesorectal excision and coloanal anastomosis or abdominoperianal resection).[4]

Therapy for stage II (T3-4 disease, without lymph node involvement) or for stage III (positive lymph node without distant metastasis) rectal cancer often include multimodal treatment with an association of neoadjuvant/adjuvant chemotherapy due to the high risk of locoregional recurrence. This risk is associated with the rectum proximity to pelvic structures and organs, the absence of serous around the rectum and the technical difficulties in having wide surgical resection margins.[4]

Survival is an essential part in the study of patients submitted to colorectal cancer treatment. Statistical analysis as survival analysis refers to the study of data related to the time of the event of interest. In other words refers to the time between one initial event when one patient or object starts one specific stage and a final event, when this stage is changed. This time is named life time or failure time and could be since death as a consequence of disease or a time until one relapse event.[5]

About 50–60% of CRC patients will develop metastasis and 80–90% of them will develop resectable metastatic liver disease. Metastatic disease frequently develops in a metachronic way after locoregional colorectal cancer treatment and liver is the most common organ involved.[4]

TMN staging is an important prognostic factor in CRC.[6] It describes the degree of tumor spread or invasion to nearby tissues, involvement of regional lymph nodes and presence of metastasis. In 1930, Dukes[7] demonstrated that ganglion metastasis presence represents an important prognostic factor related to recurrence and survival. Since then, screening of

compromised lymph nodes represents a significant procedure in anatomopathological analysis of operatory specimens from patients submitted to colorectal cancer treatment.[6]

CRC has a good prognostic when disease is diagnosed at initial stages. 5-year overall is about 55% in developed countries and 40% in developing countries. As occurs to incidence, mortality rates due to CRC are lower in women than in men worldwide, except in the Caribbean.[2]

Therefore, the aim of this study is to evaluate survival of patients with rectum cancer diagnosed and surgically treated at Cancer Reference Unit of Rio Grande do Norte State from 2007 to 2014.

## Methods

An observational retrospective study composed by 135 patients was developed at Doctor Luiz Antonio Hospital, Cancer Reference Unit of Rio Grande do Norte State, Brazil, from 2007 to 2014. The study was approved by the Research Ethics Committee (REC) from Liga Norteriograndense Contra o Câncer (Protocol 044/044/2009).

All patients more than 18 years old with rectal adenocarcinoma diagnosed by histopathology and radical surgical treatment with chemotherapy and/or radiotherapy were included in the study. Patients with others forms of cancer were excluded from this study. During the research, eleven patients were excluded due the absence of information on their records about neoadjuvant treatment, adjuvant treatment and staging.

Data were collected from the records revision considering the follow information: age, sex, origin, diagnosis, date of diagnosis (date of biopsy), TNM stage, neoadjuvant treatment, type of surgical treatment, adjuvant treatment, recurrence, death, date of death and cause of death.

All patients were submitted to surgical treatment, chemotherapy and/or radiotherapy proceeded by members of the medical staff from Doctor Luiz Antonio Hospital. Cancer staging was performed according to TNM system from American Joint Committee of Cancers (AJCC).

Overall survival was considered starting from the date of diagnosis, while disease-free survival starting from the date of surgery. Kaplan–Meier and Wilcoxon non-parametric tests were used to estimate and compare survivals, respectively. Evidence results from Wilcoxon test were evaluated considering significance level of 5%. For statistical analysis R software was used (3.2.2 version).[8,9]

## Results

From 2007 to 2014 were consulted records from 124 patients. The mean of age was 67.1 years (±15.87), with 50.3% men and 49.7% women. Considering neoadjuvant treatment, 3.2% were submitted to chemotherapy, 3.2% to radiotherapy, 37.2% performed both of them and 56.4% none of them.

Considering surgical procedures, 63.7% were submitted to abdominal retossigmoidectomy, 21.7% to rectal abdominoperianeal amputation, 6.4% to local resection and 8.06% palliative procedures. Considering adjuvant treatment, 41.12% performed chemotherapy, 7.25% radiotherapy, 19.35%

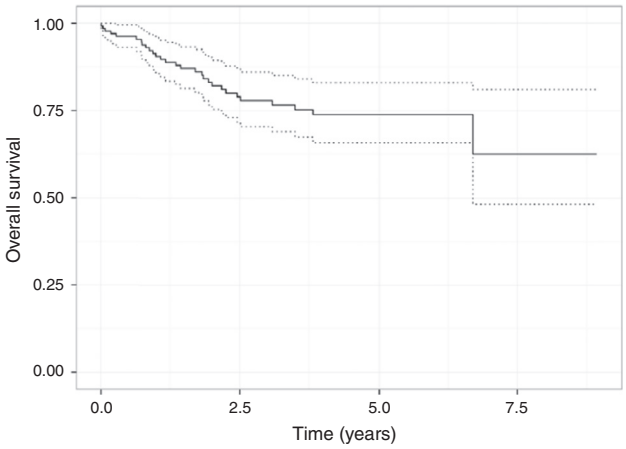


**Fig. 1 – Overall survival (solid line) and 95% confidence intervals (dashed line) estimated by Kaplan–Meier for rectal cancer data.**

performed chemotherapy associated to radiotherapy and 32.25% did not perform any of them.

Cancer recurrence occurred in 25.19% of cases. Data from patient death reveals that 34.67% died: 74.41% due to cancer, 11.62% due to cancer complications and 13.95% due to others causes.

Overall survival (Fig. 1) of patients in treatment against rectal cancer was 62% in seven years, while disease-free survival (Fig. 2) in one, three and five years was 91.7%, 75.5% and 72.1%, respectively.

Concerning age groups, we observed an increased disease-free survival in patients with age below 50 years and from 70 onwards compared to patients between 50 and 70 years of age; however, no statistical difference was evidenced ($p$-value = 0.441). Nevertheless, overall survival increases as age rises, as demonstrated when comparing patients with age below 50 years versus patients with age from 70 onwards ($p$-value = 0.008) (Fig. 3).

Regarding cancer staging, from 125 patients 18.4% were classified as stage I, 29.6% as stage II, 39.2% as stage III and

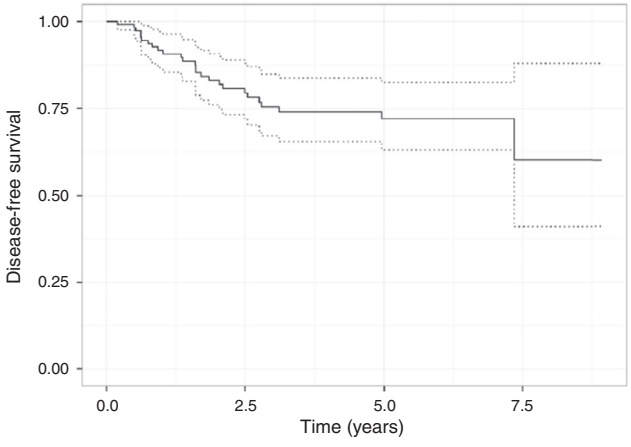


**Fig. 2 – Disease-free survival (solid line) and 95% confidence intervals (dashed line) estimated by Kaplan–Meier for rectal cancer data.**

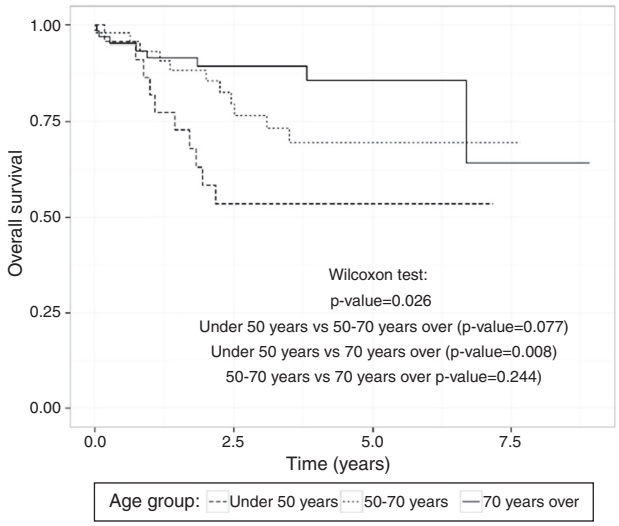


**Fig. 3 – Overall survival estimated by Kaplan–Meier for rectal cancer data comparing age groups.**

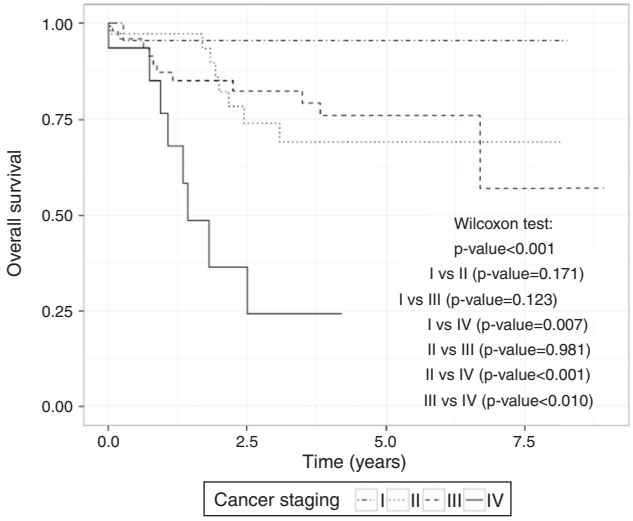


**Fig. 5 – Overall survival estimated by Kaplan–Meier for rectal cancer data comparing cancer staging.**

12.8% as stage IV. Significant difference was found between overall survivals related to cancer staging. However, only patients from stage I and II differ in a significant way considering disease-free survival (Fig. 4). On the other hand, for patients classified as stage IV it was observed a shorter overall survival, which is statistically different from others stages overall survival (Fig. 5).

In contrast, data relative to sex, surgical procedures, neoadjuvant treatment, adjuvant treatment and recurrence treatment not showed any statistical difference in overall survival and disease-free survival.

## Discussion

Distribution by sex and mean age of patients diagnosed with rectum cancer found in our study corresponds to the same features found in the literature, as well as the predominance of retossigmoidectomy as surgical treatment.

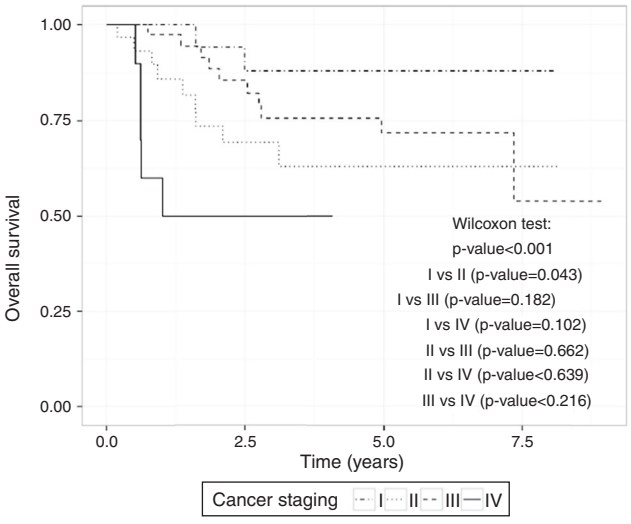


**Fig. 4 – Disease-free survival estimated by Kaplan–Meier for rectal cancer data comparing cancer staging.**

A study conducted by Pinho et al.[10] revealed a discreet prevalence in male gender, with a mean age of 61 years old, and abdominal retossigmoidectomy as the most common surgical procedure performed corresponding to 45.3% of all surgical treatments. Furthermore, it showed that from 89 patients in follow-up, 33 presented disease relapse, similar to ours results.

After a detailed analysis of data, it was observed that elderly was the age group most affected by rectal cancer, regardless of gender, and abdominal retossigmoidectomy the most common procedure. From all patients included in our study, one third died due cancer or cancer complications.

According to data analysis from Surveillance Epidemiology and End Results (SEER), survival in five years increased from 56.5% in patients diagnosed in the beginning of 1980s to 63.2% in patients diagnosed in the beginning of 1990s and recently to 64.9%. This survival increase is due mainly to early diagnosis and treatment. It is known that patient prognosis is highly dependent on the staging: in five years the overall survival is up than 90% to patients classified as Dukes A, but only 5% when they are classified as Dukes D. Unfortunately, only 10% of patients with this neoplastic disease are diagnosed early and most of them present advanced disease.[11,12]

Overall survival of patients submitted to rectal cancer treatment was 62% in seven years, while disease-free survival in one, three and five years was 91.7%, 75.5% and 72.1%, respectively. Mussnich et al.[13] evaluated overall and clinical and pathological factors related to rectal adenocarcinoma ad verified that overall in five years was 51% and 64 patients (57%) presented recurrence.

In contrast, a study performed by Downing et al.[14] identified patients diagnosed with colon and rectal cancer and classified them in a perspective of death within one month, three months and twelve months after diagnosis. Results from the latter study showed that 11.5% of patients diagnosed with colon cancer and 5.4% diagnosed with rectal cancer died

within a month after diagnosis and for both types of cancer advanced age, cancer stage at the moment of diagnosis and emergency presentation were associated with early death. Differently, our results had not showed any negative influence of advanced age in overall survival of these patients.

According to Phipps et al.,[15] comparing with patients that remained alive at the end of the follow-up or in five years after diagnosis, patients that died within five years after diagnosis were more likely to be male (58% vs. 51%) and to be smokers (64% vs. 59%). Furthermore, mortality due to distal colon cancer and rectal cancer was significantly lower than mortality due to proximal colon cancer. Although the lack of evaluation of colon cancer in the present study, it was found a significant mortality in rectal cancer patients as mentioned by Phipps et al.[15] However, ours data did not revealed difference in mortality between genders.

Considering all surgical procedures, our study did not showed any significant difference in overall survival and disease-free survival between them. Differently, according to National Comprehensive Cancer Network (NCCN), recent retrospectives comparisons between patients submitted to abdominoperianal resection and patients submitted to low anterior resection for cancer treatment revealed that former ones presented worst local control and overall survival.

## Conclusion

After a detailed analysis of data, it was observed a significant percentage of patients free from rectal cancer once overall survival and disease-free survival remained enhanced until the end of the study, suggesting that the treatment protocols used in the institution have shown to be effective.

## Conflicts of interest

The authors declare no conflicts of interest.

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