



SURVIVAL STUDY OF PATIENTS WITH NON-METASTATIC COLON CANCER

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ABSTRACT

Introduction: Colon cancer (CC) is a global and national public health issue, and understanding prognostic factors is essential for effectively tailoring treatment strategies to patients. The objective of this study is to analyze the survival of patients with non-metastatic colon cancer (NMCC) and identify the main prognostic factors. **Method:** We conducted a retrospective study at the CHUO between 2015 and 2019, based on the analysis of patient records for colon cancer. Survival was assessed using the Kaplan-Meier method, with univariate and multivariate analyses using the Log-rank test and Cox model, respectively. **Results:** We collected data on 121 patients, with a median age of 61 years (range 23-89) and a sex ratio of 1.2. The primary tumors were located in the left colon (75.2%) and right colon (24.8%). At the time of data collection, 34 deaths (28.1%) had been reported. The 3-year and 5-year disease-free survival (DFS) rates were 74.3% (95% CI, 66.3-82.3) and 67.6% (95% CI, 58.8-76.4), respectively. The median overall survival is 70 months (95% CI, 48-100) with 3-year and 5-year survival rates of 61.5% (95% CI, 54.7-68.3) and 54.8% (95% CI, 47.6-62), respectively. **Conclusion :** our results show survival data similar to those reported in the literature.

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1. Introduction

Colorectal cancer (CRC) represents a global public health problem (1). It ranked third among cancers in terms of incidence and second in terms of mortality in 2022 (1).

CC is the fourth most common cancer worldwide and the fifth in terms of mortality (1). It is the most frequent digestive cancer globally (1, 2, 3) with an incidence of 1,150,000 new cases in 2022 and a mortality rate of 576,000.

In Algeria, data from the national cancer registry network for 2022 ranks it second overall, with 7,500 cases per year (4, 5, 6).

Survival for patients with CC depends on the stage at diagnosis; a more advanced stage is associated with lower survival rates. Thus, the 5-year survival rate is 60 to 90% (7).

The treatment of NMCC relies primarily on surgical resection and medical therapy. Complete tumor resection is the main objective. The indication for adjuvant therapy depends largely on the presence of histopathological criteria, determined by the histopathological analysis of the surgical specimen (8, 9).

In Algeria, survival data for patients with NMCC are limited. This prompted our interest in conducting a retrospective study of NMCC patients with an analysis of the various prognostic factors that influenced survival (10).

2. Materials and Methods:

This is a retrospective study conducted on incident cases of NMCC diagnosed between January 1, 2015, and December 31, 2019, in the medical oncology department of the University Hospital of Oran.

The primary objective is to study the survival of patients with NMCC. Secondary objectives include determining prognostic factors and identifying the epidemiological, clinical, and histopathological profile.

Patients and Methods: All patients with a medical record who had NMCC, histologically confirmed and diagnosed between 2015 and 2019, were included in the study.

Data Collection: After completing a data collection form, we collected data from each patient's medical record.

Study Period and Duration: The vital status of each patient was determined. Patient recruitment took place from January 2015 to December 2019, with a cutoff date of June 30, 2023.

Survival Data Variables: The data required for the clinical epidemiological survival analysis are as follows:

- **Date of Origin (DO):** This corresponds to the date of histological diagnosis of non-metastatic colon cancer. All patients diagnosed between January 1, 2015, and December 31, 2019, were included in the study.

- **Date of Last Follow-up (DLF):** This is defined as the date on which the last information about the patient (alive, deceased, or lost to follow-up) was collected.

- **Follow-up time** is the time between the date of origin and the cutoff date. -**Data Point Date (DP):** This corresponds to the end date of the study. It was set for June 30, 2023.

Survival was calculated from the date of diagnosis to the date of death. For subjects who did not die, the calculation was from the date of diagnosis to the date of last follow-up (DLF).

2.1. Data Entry and Statistical Analysis

Patient survival was calculated using univariate analysis with the log-rank test; multivariate analysis was performed using the Cox proportional hazards model, and adjusted hazard ratios (HRs) were reported with their 95% confidence intervals (95% CIs). All variables with a p-value < 0.05 in univariate analysis were implemented in a multivariate Cox model. Statistical analysis of the data was performed using SPSS 20.0 software.

3. Results:

3.1. Epidemiology of colon cancer:

In total, we collected data on 121 patients with NMCC among the 323 colorectal cancer (CRC) patients meeting the study's eligibility criteria over a 5-year period. The mean age at diagnosis was 61 years, with a range from 23 to 89 years. Ninety percent of cases occurred in individuals over 45 years of age, with a male predominance and a male-to-female ratio of 1.2. NMCC accounted for 37.5% of cases in the overall population (Table 1).

Table 1: Overall patient characteristics

| features | Patients | |
|---------------------------------------|--------------|------|
| | N | % |
| Total number of patients | 121 | |
| Sex | | |
| Male | 66 | 54,5 |
| Female | 55 | 45,5 |
| Sex-ratio | 1,2 | |
| Age (years) | | |
| Median (Extrême) | 61 (23 - 89) | |
| Age ranges | | |
| ≤ 65 years | 75 | 62 |
| > 65 years | 46 | 38 |
| PS | | |
| 0-1 | 117 | 96,7 |
| 2 | 4 | 3,3 |
| Location | | |
| Left Colon | 91 | 75,2 |
| Right Colon | 30 | 24,8 |
| Primary tumor surgery | | |
| Anterior resection | 87 | 71,9 |
| Hemicolectomy | 31 | 25,6 |
| Total colectomy | 3 | 2,5 |
| Histological type | | |
| Well-differentiated ADC | 104 | 86 |
| Moderately differentiated ADC | 8 | 6,6 |
| Poorly or undifferentiated ADC | 6 | 5 |
| Mucous colloid ADC | 3 | 2,5 |
| Stade p TNM | | |
| I | 13 | 10,8 |
| II | 54 | 44,6 |
| Low risk | 20 | 16,5 |
| High risk | 34 | 28,1 |
| III | 54 | 44,6 |
| Low risk | 21 | 17,4 |
| High risk | 33 | 27,2 |

3.2. Surgical management:

All patient cases were discussed at the multidisciplinary tumor board (MDTB) of the University Hospital of Oran. A total of 121 patients with NMCC were considered for surgical management. Initial surgery was performed in 115 patients, with a mean delay of 21.6 days after diagnosis. In 6 cases, the locally advanced tumor was rendered resectable through the use of neoadjuvant chemotherapy.

3.3. pTNM Classification and Disease Stage:

The UICC pTNM classifications, 7th edition (2012) (11) and 8th edition (2017) (12), were applied for patient management. Among the 121 surgically treated cases, pTNM stage T3 was found in 79.3% of cases. Lymph node involvement was reported in the pathology report of 98 cases (81%). It was absent in 23 cases (19%). The average number of lymph nodes analyzed was 8, with a range from 1 to 46 (Table 2).

Table 2: Distribution of patients according to the pTNM classification

| Classification p TN | Patients | |
|---------------------|----------|-----|
| | N | % |
| p T1 N0 | 3 | 2,5 |
| p T2 N0-1 | 17 | 14 |

| | | |
|-----------|-----|------|
| p T3 N0-2 | 77 | 63,6 |
| p T3 Nx | 20 | 16,5 |
| p T4 N1-2 | 2 | 1,6 |
| p T4 Nx | 2 | 1,7 |
| Total | 121 | 100 |

3.4. Prognostic Groups: The study of other histopathological prognostic factors is of paramount importance, allowing for the classification of disease stages into low- and high-risk prognostic groups (13, 14, 15).

Not all of these (resection margins, histological grades and types, vasculo-lymphatic emboli, perineural invasion, tumor deposits and tumor budding) are available in all anatomopathological reports.

Tumor deposits (16, 17, 18) and tumor budding (19, 20), two recent concepts, are primarily featured in reports from 2019. In addition to these factors, emergency surgery for obstruction or perforation is considered for prognostic grouping. In our series, 44 patients were treated for obstruction and 2 patients for perforation.

4. Medical Management: Six patients with locally advanced disease were eligible for neoadjuvant chemotherapy (NACT), which allows for downstaging and enables oncological surgery of the primary tumor. NACT was administered to 98 patients with a mean interval from the first cycle of 59 ± 31.5 days (95% CI, 18–164 days), resulting in a median interval of 50 days. The CT protocols used were simplified FOLFOX 4 (54 cases), XELOX (29 cases), Capecitabine mono (11 cases), LV5FU2 (04 cases). The total number of CT cycles administered to the entire population was 939, with a mean of 9.58 ± 1.7 cycles (95% CI, 2–12 cycles) and a median of 10 cycles. The mean duration of ACT was 6.34 ± 1.5 months (95% CI, 2–11 months), with a median of 6 months. The group of 17 patients followed in outpatient care without an indication for ACT consisted of 13 patients with stage I disease, 3 patients with low-risk stage II, and one 87-year-old patient with low-risk stage III.

5. Survival Study:

The 3-year and 5-year SDS rates were 74.3% (95% CI, 66.3–82.3) and 67.6% (95% CI, 58.8–76.4), respectively (Figure 1), and the 3-year and 5-year OS rates were 85.7% (95% CI, 79.3–92.1) and 79.3 months (95% CI, 71.9–86.7), respectively (Figure 2). Analysis of SDS and OS by subgroup is illustrated in Figures 3–6.

Figure 1 : SSM curve of patients with non-metastatic colon cancer

Temps (mois)

Figure 2 : OS curve of patients with non-metastatic colon cancer

Temps (mois)

Figure 3 : SSM curves of patients according to the presence or absence of an occlusion

Temps (mois)

Figure 4 : SSM curves of patients according to disease stage

Temps (mois)

Figure 5 : SG curves of patients according to disease stage

Temps (mois)

Figure 6 : SG curves as a function of the presence or absence of recurrence

6. Analysis of Prognostic Factors:

Univariate analysis revealed a positive and significant association at the 20% level between overall survival (OS) and certain prognostic factors, namely performance status (PS) 0-1, age, presence or absence of occlusion, CEA level, and disease recurrence. Applying the Cox proportional hazards model, multivariate analysis identified independent prognostic factors associated with OS.

This analysis showed that patients with a PS 0-1 had better OS compared to those with a PS 2, with a hazard ratio (HR) of 26.24 (95% CI, 3.66–188). The difference was statistically significant ($p = 0.01$). Metastatic recurrence was associated with a poor prognosis, with an HR of 21.64 (95% CI, 7.11–65.86). The difference was highly significant ($p < 10^{-3}$).

7. Discussion

In our study, colon cancer (CC) accounted for 72.1% of colorectal cancer (CRC) cases, compared to 27.9% for rectal cancer. These proportions are consistent with data from the literature, which reports approximately two-thirds CC and one-third rectal cancer (1). Left-sided CC was clearly predominant, with 91 cases (75.2%), compared to 30 cases (24.8%) for the right colon. These results differ from data in the literature, which generally reports a more balanced distribution, with approximately 55% of cases located in the left colon and 45% in the right colon (1,2).

The distribution by sex reveals a slight male predominance (sex ratio of 1.24), which is consistent with data from the literature (21,22). The mean age at diagnosis was 61 ± 13.0 years, about ten years lower than data from Western literature, which report an age between 65 and 75 years (23, 24). This relatively young mean age compared to the literature could be an epidemiological peculiarity in the Maghreb countries, suggested in other locations, such as breast cancer.

It is established that a high PS score is associated with a poor prognosis. The 3-year survival rate for patients with a score of 0-1 was 63.3%, compared to 10% for a score ≥ 2 . This difference was highly statistically significant ($p < 0.0001$).

After 3.5 years of follow-up, 41 cases (33.8%) had experienced metastatic relapse. The survival rate in our study is similar to that found in several national studies. In the series by Hamedi Cherif (25), the 5-year survival rate was 57.2% (45.6–68.9%). Benbekhti et al. (26) reported a 5-year overall survival rate of 65%, while noting that 78/160 cases were of undetermined stage. This result should be interpreted with caution.

According to global data from the “CONCORD3” study, the 5-year colon survival rate in Algeria, from 2000 to 2014 following the participation of three cancer registries (Setif, Annaba and Batna) (27) with a 5-year OS rate of 74.25% (65.7–82.7).

In Europe, according to data from the EURO CARE 5 study (28), the 5-year survival rate was 57.0% (95% CI 56.8–57.3) (28, 29, 30).

The survival rate in the United States is among the highest, with a 5-year survival rate of 61% (31, 32).

In the series by Burton et al. (33), no difference was found in 4-year survival between right (57%) and left (52.5%) occlusions ($p=0.46$) (33).

Surgical management in the clinical presentation of occlusion was the preferred approach for a large number of patients (43.4%) compared to 14.6% in the Burton study (33). Analysis of 3-year SSM rates according to the presence or absence of occlusion was 58% (95% CI, 43–73) and 83.6% (95% CI, 75–92.2), respectively. The difference is statistically significant ($p=0.01$).

In our series, the overall survival (OS) rates according to disease stage at 30 and 60 months were stage I (91.7%, 82.5%), stage II (92.6%, 86.9%), and stage III (83%, 70.7%), respectively. Our results are consistent with those in the literature, particularly in the series by O’Connell et al. (34), who reported 30-month and 60-month survival rates closely related to disease stage: Stage I (96.1–93.2%), Stage II (89.2–82.5%), and Stage III (72.7–59.5%).

Conclusion

This is a retrospective observational study. It was impossible to retrieve certain data from medical records. The study involved a relatively small number of patients, but one comparable to series published in the literature. Our patients were relatively younger compared to data from Western countries. The particularly high frequency of colon cancers revealed by acute intestinal obstruction reflects the diagnostic delay. Insufficient data from the histopathological report of the surgical specimens makes therapeutic management of patients difficult. Analysis of survival results compared to data from the Maghreb and Western literature shows variability in the figures. The results should be interpreted with caution. Their interpretation is difficult due to the different characteristics of the studied populations. The establishment of a mortality register will be a major asset in evaluating future public health screening initiatives.

References

- (1) Bray, F., Laversanne, M., and al (2024). Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: a cancer journal for clinicians*, 74(3), 229-263.
- (2) Arnold M, Abnet CC, et al. Global Burden of 5 Major Types of Gastrointestinal Cancer. *Gastroenterology*. juill 2020;159(1):335-349.e15.
- (3) Safiri S, Sepanlou SG, et al. The global, regional, and national burden of colorectal cancer and its attributable risk factors in 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *The Lancet Gastroenterology & Hepatology*. déc 2019;4(12):913-33.
- (4) Kara L ; Meguenni.K ; Données du Réseau National des Registres du Cancer 2021-2022. 30/10/2024.
- (5) Boutekdjiret. L. Bouheraoua. A ; A. Données du Réseau Centre des Registres du Cancer 2021-2022. 30/10/2021
- (6) Bouheraoua. A ; Bouamra. A and AL. Tendances Evolutive des Cinq premiers Cancers à Alger 2002-2021. Institut National de San-

té Publique.

- (7) Tong GJ, Zhang GY, et al. Comparison of the eighth version of the American Joint Committee on Cancer manual to the seventh version for colorectal cancer: A retrospective review of our data. *WJCO*. 10 nov 2018;9(7):148-61.
- (8) National Comprehensive Cancer Network (NCCN). Clinical practice guidelines in oncology. October 27, 2022.
- (9) Argilés G, Taberero J, et al. Localised colon cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Annals of Oncology*. oct 2020;31(10):1291-305.
- (10) Plan national cancer Algérie 2015-2019.
- (11) Hari DM, Leung AM et al. AJCC Cancer Staging Manual 7th Edition Criteria for Colon Cancer: Do the Complex Modifications Improve Prognostic Assessment? *Journal of the American College of Surgeons*. août 2013;217(2):181-90.
- (12) Amin MB, Greene FL et al. The Eighth Edition AJCC Cancer Staging Manual: Continuing to build a bridge from a population-based to a more “personalized” approach to cancer staging: The Eighth Edition AJCC Cancer Staging Manual. *CA: A Cancer Journal for Clinicians*. mars 2017;67(2):93-9.
- (13) Chu QD, Zhou M. Positive surgical margins contribute to the survival paradox between patients with stage IIB/C (T4N0) and stage IIIA (T1-2N1, T1N2a) colon cancer. *Surgery*. nov 2016;160(5):1333-43.
- (14) Kim MJ, Jeong SY, et al. Survival Paradox Between Stage IIB/C (T4N0) and Stage IIIA (T1-2N1) Colon Cancer. *Ann Surg Oncol*. févr 2015;22(2):505-12.
- (15) Gunderson LL, Jessup JM, Revised TN Categorization for Colon Cancer Based on National Survival Outcomes Data. *JCO*. 10 janv 2010;28(2):264-71.
- (16) Mayo E, Llanos AAM, Prognostic value of tumour deposit and perineural invasion status in colorectal cancer patients: a SEER-based population study. *Histopathology*. août 2016;69(2):230-8.
- (17) Lo DS, Pollett A, Prognostic significance of mesenteric tumor nodules in patients with stage III colorectal cancer. *Cancer*. 1 janv 2008;112(1):50-4.
- (18) Ueno H, Mochizuki H, et al. Extramural Cancer Deposits Without Nodal Structure in Colorectal Cancer: Optimal Categorization for Prognostic Staging. *Am J Clin Pathol*. févr 2007;127(2):287-94.
- (19) Lee VWK, Chan KF. Tumor budding and poorly-differentiated cluster in prognostication in Stage II colon cancer. *Pathology - Research and Practice*. mars 2018;214(3):402-7.
- (20) Romiti A, Roberto M, et al. Study of histopathologic parameters to define the prognosis of stage II colon cancer. *Int J Colorectal Dis*. mai 2019;34(5):905-13.
- (21) Center MM, Jemal A, Worldwide Variations in Colorectal Cancer. *CA: A Cancer Journal for Clinicians*. 1 nov 2009;59(6):366-78.
- (22) Levi F, Randimbison L, Trends in the subsite distribution of colorectal carcinomas and polyps: An update. *Cancer*. 1 nov 1998;83(9):2040-2.
- (23) Hammouda D, Boutekdjiret L. Surveillance épidémiologique des cancers : Résultats préliminaires nationaux. :10.
- (24) Institut national du cancer : Epidémiologie des cancers - de nouvelles données d'incidence la période 1990 -2023.
- (25) M HC, E B et al. Cancer estimation of incidence and survival in Algeria 2014. *J Cancer Res Ther*. 1 oct 2015;3(9):100-4.
- (26) Abdrebbi SB, Meguenni K. Survie sur 05 ans des cancers colorectaux dans la Wilaya de Tlemcen.
- (27) Allemanni C, Matsuda T et al. Global surveillance of trends in cancer survival 2000–14 (CONCORD-3): analysis of individual records for 37 513 025 patients diagnosed with one of 18 cancers from 322 population-based registries in 71 countries. *The Lancet*. mars 2018;391(10125):1023-75.
- (28) De Angelis R, Sant M et al. Cancer survival in Europe 1999–2007 by country and age: results of EUROCARE-5—a population-based study. *The Lancet Oncology*. janv 2014;15(1):23-34.
- (29) Holleczeck B, Rossi S, et al. On-going improvement and persistent differences in the survival for patients with colon and rectum cancer across Europe 1999–2007 – Results from the EUROCARE-5 study. *European Journal of Cancer*. oct 2015;51(15):2158-68.
- (30) Survie des personnes atteintes de cancer en France métropolitaine 1989 2018 Colon Rectum.
- (31) Surveillance, Epidemiology, and End Results (SEER) Stat Database, Nov 2015 Sub (1973–2013 varying).
- (32) SEER*Explorer: An interactive website for SEER cancer statistics. Surveillance Research Program, National Cancer Institute. November 01 2018.
- (33) Burton S, Norman AR. Predictive poor prognostic factors in colonic carcinoma. *Surgical Oncology*. août 2006;15(2):71-8.
- (34) O’Connell JB, Maggard MA. Colon Cancer Survival Rates With the New American Joint Committee on Cancer Sixth Edition Staging. *JNCI Journal of the National Cancer Institute*. 6 oct 2004;96(19):1420-5.