Comparison of epidemiological criteria for colorectal cancer over 10 years: incidence, therapeutic management and overall survival

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ABSTRACT

Colorectal Cancer (CRC) is ranked among the most common cancers in the world, third after breast and prostate cancer and second digestive cancer in Morocco after gastric cancer. However, its incidence in our country remains lower than that of Western countries (2.5 to 3.3/100,000 ha). Knowledge of the epidemiological characteristics of CRC will certainly condition our therapeutic attitudes. The aim of this article is to compare the epidemiological, anatomopathological and therapeutic characteristics over ten years and to show that progress in recent years in terms of treatment has contributed to the increase in survival rates. We included 571 patients in a retrospective study with CRC treated at the medical oncology department of Fez over a period from June 2014 to June 2023. The Kaplan Meier method was used to estimate the median survival. There is a slight male predominance. The average age in our study at the time of diagnosis was 59 years. The time between the onset of symptoms and the consultation was mostly more than 6 months between the first two years of the study and was less than 3 months in the last two years. Clinical symptoms were dominated by transit disorders, rectal bleeding and weight loss. Median Overall Survival (OS) was 22.3 months ± 0.6 CI (21-23.6) between 2014-2016 *vs.* 28.3 months ± 0.6 CI (24-29.6) between 2021-2023. We reported an improvement in Progression Free Survival (PFS) in the last two years (192 months ± 0.6 CI (19–21) *vs.* 16,4 months ± 0.4 CI (16-20). Our study showed an increase in overall survival and progression free survival over the past ten years.

Keywords: colorectal cancer, comparison, survival

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INTRODUCTION

Colorectal Cancer (CRC) is the third most commonly diagnosed cancer, after prostate and lung cancer, in men, and the fourth, after breast, cervical, and thyroid cancer in women. The variability of CRC incidence in time and space suggests an important influence of environmental factors. First of all, alcohol and tobacco are associated with an increased risk of CRC [1-3]. Diet, metabolic syndrome and physical activity are also associated with risk modification. Indeed, protein consumption appears to be linked to an increased risk of CRC. Data on meat consumption are conflicting, with the risk being more related to excessive consumption of red meat [4, 5]. Regular physical activity would reduce the risk of CRC. High caloric intake, obesity and physical inactivity are associated with an increased risk of adenomas or CRC [6-8]. Finally, type 2 diabetes is also a risk factor for CRC [9]. Its incidence is significantly higher in men than in women. After breast and cervical cancer screening, colorectal cancer screening has been developed, and an increasing number of countries have organized systematic screening targeting the population between 50 years and 70 years of age. All stages combined, the 5 years survival for colon cancer is around 60% [10, 11]. 40%-60% of patients will become metastatic. The purpose of this work is to show advances in colorectal cancer diagnosis and treatment, including chemotherapy, targeted therapy, immunotherapy, and wider and faster access to these treatments have contributed to increase survival rates over the past decade.

MATERIALS AND METHODS

This is a retrospective study of 571 patients with colorectal cancer at all stages, collected in the medical oncology department of the Hassan II university hospital center in Fez during a 10-years period from June 2014 to June 2023. We compared the characteristics of tow groups: Group A between 2014-2016, and Group B between 2021-2023. Statistical analysis of the data was performed using Microsoft Office Excel and SPSS software. Qualitative variables were expressed as a percentage and quantitative variables were expressed as an average. Kaplan-Meier analysis was used to determine overall and progression-free survival rates.

RESULT

564 patients with CRC were identified in the patient register of the medical oncology department at the Hassan II Hospital in Fez. We reported a higher number of patients in the last two years: 146 cases (Figure 1).
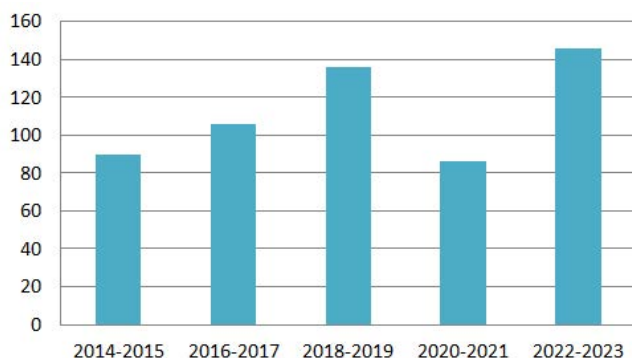
Fig. 1. Distribution of patients by years

According to our results, there is a slight male predominance with 293 men and 271 women and a sex ratio (M/F) of 1.08 in the general population. For colon cancers, there are 207 men affected (57% of cases) and 157 women (43%) with a sex ratio (M/F) of 1.31. For rectal cancers, 104 (52%) women were diagnosed during this period *vs.* 96 men (48%) with a sex ratio (M/F) of 0.92. The mean age in our study at the time of diagnosis was 59 years with ex-tremes ranging from 16 years to 103 years. The majority age group was 61 years to 70 years old. Among the 564 patients, 291 patients were aged under 60 years (51.59%).The main personal histories observed in our study are tobacco and excessive consumption of meat found in 150 patients and 138 patients respectively. Alco-hol consumption, history of adenoma, Crohn's disease and obe-sity were objectified in 36 patients, 28 patients, 15 patients and 70 patients respectively. The time between the onset of symptoms and the consultation was mostly more than 6 months between the first two years of the study. There has been a clear reduction in the consultation period over the past two years. The factors that mo-tivated the consultation were most often the association of several clinical signs. The clinical symptoms were dominated by transit disorders, rectal bleeding and weight loss (Table 1).

Tab. 1. The main clinical signs in patients	**Clinical Signs**	**Number**	**%**
	Transit disorders	287	51.51
	(Diarrhea, Constipation or Alternation Diarrhea/constipation)		
	Rectal bleeding	276	49.24
	Weight loss	270	48.48
	Abdominal pain	118	21
	rectal syndrome	101	18.18
	(Crushing, Tenesmus, false needs and incomplete evacuations)		
	Vomiting	29	5.30
	Discomfort while sitting	21	3.79

In our study, 120 patients (21%) were in good general condition (PS 1), 360 patients (64%) were PS 2 and 54 patients and 28 pa-tients were PS 3 and PS 4 respectively. There is a predominance of lieberkuhnian adenocarcinoma (88%) compared to other types of cancer (mucinous carcinomas), with a predominance of stages IV in the general population. There has been a significant increase in the number of patients with stage II colon cancer over the past two years (2021-2023) compared to 2014-2016. The elective site of metastases was in descending order: liver, lung, peritoneum and bone. Tumor marker assay was performed in 476 cases (84.3%). In 146 patients (26%), liver function tests were disturbed. Rec-to-colonoscopy made it possible to objectify the appearance and extent of the primary tumour. There is a predominance of veg-etative forms with a number of 237 patients or 42.1%. Thoraco-abdomino-pelvic Computed Tomography (CT) was performed in all patients. Metastases were localized in liver, lung, peritoneal and bone in 82 patients, 76 patients, 45 patients and 12 patients respectively (Table 2).

Tab. 2. Comparison of patients characteristics over the years (2014-2016/2021-2023)		**Group 1 (2014-2016)**	**Group 2 (2021-2023)**
	Middle age (years)	59.7	51.6
	Performance Status (PS)		
	1	61	106
	2	50	87
	3	85	39
	Mode of Metastasis (%)		
	Metachrone	45.3	60.3
	Synchronous	57.7	39.7

Site of Metastases (%)		
Liver	44.1	52
Lung	3.4	4.6
Peritoneum	23.7	15.3
Bones	1.7	1.5
liver enzymes (%)		
Normal	70.2	81.3
Pathological	25.5	16.4
Carcinoembryonic Antigen (CEA) (%)		
Normal	60	59.1
Pathological	40	39.9

Abdominal Magnetic Resonance Imaging (MRI) was performed in patients with liver metastases in 36 cases (21%). In 12 cases (32%), the enhancement of the lesion after injection of gadolinium was peripheral producing a target image. There is an increase in the performance of abdominal MRI between the period 2021-2023 (32 cases) compared to 2014-2016 (04 cases). We reported an increase in patients with high-risk stage III 44 patients+(59.45%) during the period 2021-2023 *vs.* 14 patients (28%) between 2014-2016. We have observed an improvement in overall survival in patients who have received a combination of chemotherapy+biotherapy in recent years with a very significant $p < 0.001$ (Table 3 and Figure 2). An increase in progression free survival was also observed ($p = 0.02$) (Figure 3). Median Over-all Survival (OS) was 22.3 months $\pm$ 0.6 CI (21-23.6) between 2014-2016 *vs.* 28.3 months $\pm$ 0.6 CI (24-29.6) between 2021- 2023. We reported an improvement in Progression Free Survival (PFS) in the last two years (19.2 months $\pm$ 0.6 CI (19-21) *vs.* 16.4 months $\pm$ 0.4 CI (16-20).

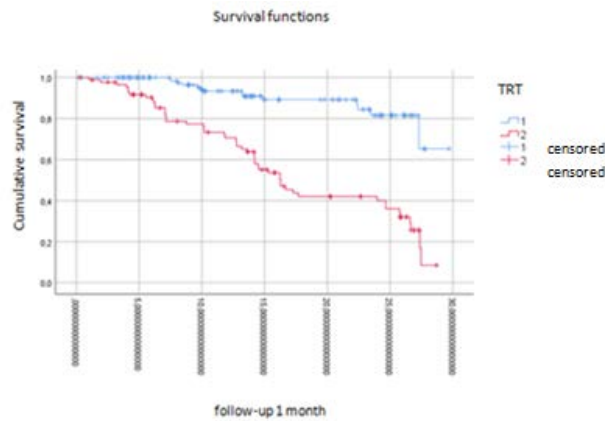| **Tab. 3.** Overall comparisons		Khi-carre	DDL	Sig.
	Log Rank (Mantel-Cox)	224.491	1	0.001

Fig. 2. Overall survival curve depending on treatment received (chemotherapy with or without biotherapy) in patients with stage IV in the last two years of our study

Coding:
1. Chemotherapy+biotherapy
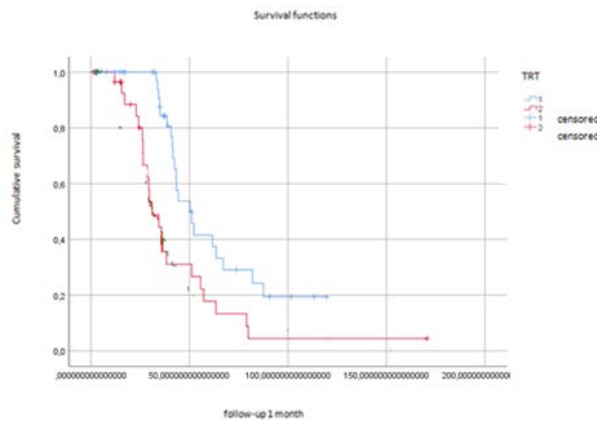2. Chemotherapy alone

Fig. 3. Progression free survival curve depending on treatment received (chemotherapy with or without biotherapy) in patients with stage IV in the last two years of our study

Coding:
1. Chemotherapy+biotherapy
2. Chemotherapy alone

DISCUSSION

Morocco is considered a high risk country for colorectal cancer, with a lower incidence compared to Europe. The decrease in mortality, observed as well as the improvement in overall survival and progression-free survival observed in recent years can be explained by a diagnosis of cancers at an earlier stage, but also by improving treatment: surgical technique and adjuvant chemotherapy in particular [12]. The evolution of net survival is the consequence of greater precocity from stage to diagnosis combined with improvement in therapeutic practice. Various studies describe an increased risk of developing colorectal cancer linked to the Western life style. More precisely, are considered as factors risk obesity, sedentary behavior and a diet rich in meat and consumption of alcohol and smoking. There are also the existence of "not modifiable" risk factors: age, history of adenoma, extensive inflammatory colitis and genetic mutation (lynch syndrome and familial adenomatous polyposis).

Determination of tumor molecular status (RAS, BRAF and MSI) is essential from the start of treatment. The genetic study in search of a mutation of the KRAS gene is essential before the introduction of a biotherapy. Indeed, the mutation of the KRAS gene confers resistance to anti EGFR [13, 14]. The combination of targeted therapies with Chemotherapy (CT) provides a better overall response. The molecules used are monoclonal antibodies:

- Anti-vascular endothelial growth factor: Bevacizumab.
- Anti-epidermal growth factor receptor: Panitumumab and Cetuximab.

The search for Microsatellite Instability (MSI) and/or deficiency of the MMR system must be systematic. The presence of a dMMR/MSI status confers particular sensitivity to immunotherapy regardless of the laterality of the primary tumor and the BRAF status. This was confirmed by the phase III trial (KEYNOTE 177) with Pembrolizumab as first-line treatment with a PFS of 16.5 months and objective response rates reaching 43.8% [15]. The presence of a BRAF V600E mutation has a poor prognosis. Of the exploratory data on small numbers providing a benefit in terms of overall survival with a tri chemotherapy+Bevacizumab [16]. Several studies have shown that cancer laterality is a prognostic factor independent of mutation status in metastatic colon cancer, with a poor prognosis for right colon cancers [17]. Current data concerning the influence of tumor location (right/left colon) in the therapeutic choice suggest a predictive effect of anti-EGFR efficacy in terms of response, and OS for left colon cancers and conversely a trend towards better efficacy of Bevacizumab in terms of OS for right colon cancer [18, 19]. In addition, a phase III trial recently showed equivalent efficacy in terms of response and PFS between a bichemotherapy or trichemotherapy associated with an anti EGFR for left colon cancer RAS/BRAF WT [20].

In our study, the survival rates for patients with colorectal cancer between 2014-2016 are lower than the period between 2021-2023. This difference is due to the influence of several factors which are in the first rank the use of more effective treatment precisely in terms of chemotherapy and targeted therapy.

CONCLUSION

This study demonstrated an enhancement in diagnostic delays and treatment outcome for colorectal cancer. More efforts are warranted to improve access to new drugs in advanced stages.

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