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**Analytical Epidemiological Study of Dietary and Environmental Risk
Factors Associated with Colorectal Cancer in Relizane, Algeria**

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Dedication

To myself, to the one who fought her battles in silence, stumbled many times, yet rose again every single time. To the long nights where exhaustion mixed with hope, and to the heart that never gave up despite all the pressure...

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Asnoui Imane

Dedication



The completion of this dissertation marks the culmination of a 17-year educational journey. Looking back to when I first started as a child, it feels surreal to have reached this definitive milestone. These long years of study have been a profound journey of self-discovery—filled with immense highs, challenging lows, and invaluable lessons that extended far beyond the classroom. I am deeply grateful for every experience that shaped me into the person I am today, and this achievement would not have been possible without the guidance and unwavering support of many extraordinary people.

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Bensahli Akrame

Abstract

Introduction

Colorectal cancer (CRC) is one of the most common cancers worldwide and in Algeria. Its development results from a complex interaction between genetic, environmental, dietary, and lifestyle factors.

Objective

This study aimed to identify and evaluate the main risk factors associated with colorectal cancer by comparing patients with CRC to healthy control subjects.

Materials and methods

This is an observational case-control study with a descriptive and analytical design, conducted in the oncology department of Ahmed Francis Hospital (Oued Rhiau, Relizane, Algeria) from February to May 2026. A total of 202 participants were included (162 cases and 40 controls). Data were collected using a standardized questionnaire and analyzed using SPSS version 27. The level of statistical significance was set at $p < 0.05$.

Results

Significant associations were found between CRC and several studied factors. Non-modifiable factors, including age, family history, inflammatory bowel disease, and colorectal polyps, were strongly associated with the disease ($p < 0.001$). Among modifiable factors, obesity, smoking, chronic stress, and certain dietary habits were significantly associated with CRC. No significant association was observed for red meat consumption, green vegetable intake, or fiber intake. Clinical and disease-related parameters, including TNM stage, metastasis, tumor location, symptoms, and delay before consultation, were also significantly associated with CRC ($p < 0.001$).

Conclusion

Colorectal cancer is a multifactorial disease involving both modifiable and non-modifiable risk factors. Prevention is based on a healthy lifestyle and early screening to reduce its incidence and improve prognosis.

Keywords: Colorectal -cancer Risk factors - Case-control study- Lifestyle factors- Prevention

Résumé

Introduction

Le cancer colorectal (CCR) figure parmi les cancers les plus fréquents dans le monde et en Algérie. Son développement résulte d'une interaction complexe entre des facteurs génétiques, environnementaux, alimentaires et liés au mode de vie.

Objectif

Cette étude visait à identifier et à évaluer les principaux facteurs de risque associés au cancer colorectal, à travers une comparaison entre des patients atteints et des sujets témoins sains.

Matériels et méthodes

Il s'agit d'une étude observationnelle de type cas-témoins, à visée descriptive et analytique, réalisée au service d'oncologie de l'hôpital Ahmed Francis d'Oued Rhiau (Relizane, Algérie) entre février et mai 2026, incluant 202 participants (162 cas et 40 témoins). Les données ont été recueillies à l'aide d'un questionnaire standardisé et analysées avec SPSS version 27. Le seuil de signification statistique a été fixé à $p < 0,05$.

Résultats

Des associations significatives ont été observées entre le CCR et plusieurs facteurs étudiés. Les facteurs non modifiables (âge, antécédents familiaux, maladies inflammatoires chroniques de l'intestin et polypes colorectaux) étaient fortement associés à la maladie ($p < 0,001$). Parmi les facteurs modifiables, l'obésité, le tabagisme, le stress chronique ainsi que certaines habitudes alimentaires étaient significativement associés au CCR. En revanche, aucune association significative n'a été retrouvée pour la consommation de viande rouge, de légumes verts et l'apport en fibres. Les paramètres cliniques et évolutifs (stade TNM, métastases, localisation tumorale, symptômes et délai de consultation) étaient également fortement associés au CCR ($p < 0,001$).

Conclusion

Le cancer colorectal est une pathologie multifactorielle impliquant des facteurs de risque modifiables et non modifiables. La prévention repose sur l'adoption d'un mode de vie sain et le dépistage précoce, afin de réduire son incidence et d'améliorer le pronostic.

Mots-clés : Cancer colorectal – Facteurs de risque – Étude cas-témoins – Facteurs liés au mode de vie – Prévention

الملخص

المقدمة:

يُعد سرطان القولون والمستقيم (CRC) من أكثر أنواع السرطان شيوعاً عالمياً وفي الجزائر، وينتج تطوره عن تفاعل معقد بين عوامل وراثية وبيئية وغذائية وعوامل مرتبطة بنمط الحياة.

الهدف:

هدفت هذه الدراسة إلى تحديد وتقييم أهم عوامل الخطر المرتبطة بسرطان القولون والمستقيم من خلال مقارنة المرضى المصابين بهذا السرطان مع أفراد أصحاء (شواهد).

المواد

والطرق:

أُجريت هذه الدراسة الرصدية من نوع الحالات والشواهد (Case-Control)، ذات الطابع الوصفي والتحليلي، بمصلحة علم الأورام بمستشفى أحمد فرانسيس بوادي رهيو (ولاية غليزان، الجزائر)، خلال الفترة الممتدة من فبراير إلى مايو 2026. شملت الدراسة 202 مشاركاً، منهم 162 حالة و40 شواهداً. جُمعت البيانات باستخدام استبيان معياري، وحُللت باستعمال برنامج SPSS الإصدار 27، مع اعتماد مستوى الدلالة الإحصائية عند $(p < 0.05)$.

النتائج:

أظهرت النتائج وجود ارتباطات ذات دلالة إحصائية بين سرطان القولون والمستقيم وعدة عوامل مدروسة. فقد ارتبطت العوامل غير القابلة للتعديل، مثل التقدم في العمر، والتاريخ العائلي للمرض، وأمراض الأمعاء الالتهابية المزمنة، وسلائل القولون والمستقيم، ارتباطاً قوياً بالإصابة بالمرض. $(p < 0.001)$ كما أظهرت العوامل القابلة للتعديل، مثل السمنة والتدخين والتوتر المزمن وبعض العادات الغذائية، ارتباطاً ذات دلالة إحصائية مع المرض. في المقابل، لم تُسجل علاقة ذات دلالة إحصائية بين الإصابة بالمرض واستهلاك اللحوم الحمراء أو الخضار أو الألياف الغذائية. كذلك ارتبطت المؤشرات السريرية وتطور المرض، مثل مرحلة TNM، ووجود النقائل، وموقع الورم، والأعراض السريرية، وتأخر الاستشارة الطبية، ارتباطاً معنوياً بسرطان القولون والمستقيم. $(p < 0.001)$

الخلاصة:

يُعد سرطان القولون والمستقيم مرضاً متعدد العوامل، يتأثر بعوامل خطر قابلة للتعديل وأخرى غير قابلة للتعديل. وتُعد الوقاية القائمة على تبني نمط حياة صحي والكشف المبكر من أهم الاستراتيجيات للحد من حدوث المرض وتحسين إنذاره.

الكلمات

المفتاحية:

سرطان القولون والمستقيم؛ عوامل الخطر؛ دراسة الحالات والشواهد؛ نمط الحياة؛ الوقاية.

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LIST OF ABBREVIATIONS

Abbreviation	Full Term
17p	Short arm (p arm) of chromosome 17
18q	Long arm (q arm) of chromosome 18
3D	Three-Dimensional
3rd	Third
5-FU	5-Fluorouracil
APC	Adenomatous Polyposis Coli
BAX	BCL2 Associated X protein
BMC Cancer	BioMed Central Cancer
BMI	Body Mass Index
BRAF	B-Raf proto-oncogene, serine/threonine kinase
CEA	Carcinoembryonic Antigen
CIMP	CpG Island Methylator Phenotype
CIN	Chromosomal Instability
CIRC	Colorectal Interdisciplinary Review Committee
Cl⁻	Chloride
CLs	Confidence Limits
cm	Centimeter
CpG	Cytosine–phosphate–Guanine (dinucleotide)
CRC	Colorectal Cancer
CRCs	Colorectal Cancers
CRM	Circumferential Resection Margin
CT	Computed Tomography
CT Colonography	Computed Tomography Colonography
CT Scan	Computed Tomography Scan
DCBE	Double Contrast Barium Enema
dMMR	Deficient DNA Mismatch Repair
DNA	Deoxyribonucleic Acid
DNA-FIT	DNA–Fecal Immunochemical Test
e.g.	Exempli gratia
EFSA	European Food Safety Authority
EGFR	Epidermal Growth Factor Receptor
EPCAM	Epithelial Cell Adhesion Molecule
Epi proColon	Plasma-based SEPT9 DNA methylation test
ESMO	European Society for Medical Oncology
etc.	Et cetera
EUS	Endoscopic Ultrasound
FAP	Familial Adenomatous Polyposis
FIT	Fecal Immunochemical Test
GALT	Gut-Associated Lymphoid Tissue
gFOBT	Guaiac-based Fecal Occult Blood Test
GISTs	Gastrointestinal Stromal Tumors
HCAs	Heterocyclic Amines
HDI	Human Development Index

LIST OF ABBREVIATION

HER2	Human Epidermal Growth Factor Receptor 2
HNPCC	Hereditary Non-Polyposis Colorectal Cancer
IARC	International Agency for Research on Cancer
IBD	Inflammatory Bowel Disease
IBM SPSS	IBM Statistical Package for the Social Sciences
iFOBT	Immunochemical Fecal Occult Blood Test
IGF-1	Insulin-like Growth Factor 1
IGF2R	Insulin-like Growth Factor 2 Receptor
IL-17	Interleukin-17
IMA	Inferior Mesenteric Artery
INCa	National Cancer Institute (France)
K⁺	Potassium
kg	Kilogram
kg/m²	Kilogram per square meter
KRAS	Kirsten Rat Sarcoma Viral Oncogene Homolog
L1	First Lumbar Vertebra
L3	Third Lumbar Vertebra
M	Metastasis
m	Meter
M0	No Distant Metastasis
M1	Presence of Distant Metastasis
M1a	Distant metastasis confined to one organ or site
M1b	Distant metastases involving more than one organ or site
MALT	Mucosa-Associated Lymphoid Tissue
MAPK	Mitogen-Activated Protein Kinase
MD	Doctor of Medicine
MLH1	MutL Homolog 1
MMR	Mismatch Repair
MRI	Magnetic Resonance Imaging
MSH2	MutS Homolog 2
MSH6	MutS Homolog 6
MSI	Microsatellite Instability
MSI-H	Microsatellite Instability–High
N	Node
n	Number of Patients
N0	No Regional Lymph Node Metastasis
N1	Metastasis in 1–3 Regional Lymph Nodes
N1a	Metastasis in One Regional Lymph Node
N1b	Metastasis in Two to Three Regional Lymph Nodes
N1c	Tumor deposits without regional lymph node metastasis
N2	Metastasis in 4 or More Regional Lymph Nodes
N2a	Metastasis in 4–6 Regional Lymph Nodes
N2b	Metastasis in 7 or More Regional Lymph Nodes
Na⁺	Sodium
NCI	National Cancer Institute
NOVA	Food Classification System Based on Processing
NTRK	Neurotrophic Tyrosine Receptor Kinase
Omega-3s	Omega-3 Fatty Acids

LIST OF ABBREVIATION

Omega-6	Omega-6 Fatty Acids
ORs	Odds Ratios
p (p-value)	Probability Value
PAHs	Polycyclic Aromatic Hydrocarbons
pH	Potential of Hydrogen
PI3K	Phosphoinositide 3-Kinase
pM	Pathological Distant Metastasis
PMS2	Postmeiotic Segregation Increased 2
pN	Pathological Regional Lymph Nodes
PNNS	National Nutrition and Health Program
POPs	Persistent Organic Pollutants
pT	Pathological Primary Tumor
pT Stage	Pathological Tumor Stage
r	Pearson Correlation Coefficient
RAS-RAF-MAPK Pathway	Rat Sarcoma–Rapidly Accelerated Fibrosarcoma–Mitogen-Activated Protein Kinase Pathway
RNV3P	Réseau National de Vigilance et de Prévention des Pathologies Professionnelles
RR	Relative Risk
S	Since
S3	Third Sacral Vertebra
SBRT	Stereotactic Body Radiotherapy
SCFAs	Short-Chain Fatty Acids
sDNA-FIT	Stool DNA-FIT
SMA	Superior Mesenteric Artery
SMAD2/4	Mothers Against Decapentaplegic Homolog 2/4
SORD	Sorbitol Dehydrogenase
T	Tumor
T1	Tumor Invading Submucosa
T1D	Type 1 Diabetes Mellitus
T2	Tumor Invading Muscularis Propria
T2D	Type 2 Diabetes Mellitus
T3	Tumor Invading Through Muscularis Propria
T4	Tumor Invading Visceral Peritoneum and/or Adjacent Organs
T4a	Tumor Perforates the Visceral Peritoneum
T4b	Tumor Invades Adjacent Organs or Structures
TGFB1-SMAD Pathway	Transforming Growth Factor Beta 1–SMAD Signaling Pathway
TGFBR2	Transforming Growth Factor Beta Receptor 2
TGF-β	Transforming Growth Factor Beta Signaling
Tis	Tumor in situ (Carcinoma in situ)
TM	Trademark
TME	Total Mesorectal Excision
TNM	Tumor–Node–Metastasis
TP53	Tumor Protein p53
UT MD Anderson Cancer Center	The University of Texas MD Anderson Cancer Center
VEGF	Vascular Endothelial Growth Factor
Vitamin B	Group of Water-Soluble Vitamins (B Complex)

LIST OF ABBREVIATION

Vitamin D	Calciferol
Vitamin K	Vitamin Koagulation
WCRF/AICR	World Cancer Research Fund / American Institute for Cancer Research
WHO	World Health Organization
Wnt/β-catenin Pathway	Wingless-related Integration Site / Beta-catenin Signaling Pathway
WNT-APC-CTNNB1 Pathway	Wingless-related Integration Site–Adenomatous Polyposis Coli–Catenin Beta 1 Pathway
X-ray	X-radiation
χ^2	Chi-squared Test

Introduction

Introduction

Colorectal cancer (CRC) represents a major global public health issue due to its high incidence and mortality rates. In 2022, more than 1.9 million new cases and approximately 904,000 deaths were recorded worldwide, making CRC the third most commonly diagnosed cancer and the second leading cause of cancer-related deaths globally (IARC, 2024).

In Algeria, the incidence of colorectal cancer has been steadily increasing. According to GLOBOCAN 2022, CRC ranks as the second most common cancer after breast cancer. In men, it is the second most diagnosed cancer after lung cancer, while in women it ranks after breast cancer. More than 6,500 new cases are diagnosed annually. This increase is associated with population aging, urbanization, dietary changes, and the adoption of a Western lifestyle characterized by physical inactivity, obesity, and smoking (WHO, 2024).

Colorectal cancer is defined as a malignant proliferation of epithelial cells in the colon or rectum. It generally results from the progressive transformation of adenomatous polyps through the adenoma–carcinoma sequence. Its pathophysiology involves the accumulation of genetic alterations affecting particularly the APC, KRAS, and TP53 genes, leading to dysregulation of cell proliferation, reduced apoptosis, and genomic instability that promotes tumor invasion and metastasis (Fearon & Vogelstein, 1990; BMC Cancer, 2025). Chronic inflammation, oxidative stress, and alterations in the intestinal microbiota also contribute to colorectal carcinogenesis.

The development of CRC depends on several genetic, environmental, and behavioral factors. The main risk factors include advanced age, family history, chronic inflammatory bowel diseases, a diet rich in red meat and animal fats and low in fiber, as well as smoking, alcohol consumption, and physical inactivity (National Cancer Institute, 2024). Obesity and metabolic syndrome also increase the risk of developing this disease (WHO, 2024).

Despite significant advances in diagnosis and treatment, the prognosis of colorectal cancer remains strongly dependent on the stage at diagnosis, highlighting the importance of early screening and identification of risk factors.

In this context, our study conducted in the oncology department aimed to identify the main risk factors associated with colorectal cancer through a descriptive cross-sectional study and an analytical case-control study comparing patients with CRC to healthy control subjects.

Literature Review

CHAPTER I

Anatomy and Physiology of the Colorectal Complex

1. Descriptive anatomy of the colorectal segment

The large intestine, or colon, is the terminal portion of the digestive tract, beginning at the ileocecal valve where it receives the contents of the small intestine and extending for an average length of approximately 1.5 meters to the rectum and anal canal. It is anatomically divided into the cecum, ascending colon, transverse colon, descending colon, sigmoid colon, and rectum, with certain segments suspended by mesenteries, while others are retroperitoneal and relatively fixed. Its main physiological function is the reabsorption of water and electrolytes, which transforms the liquid chyme from the small intestine into a more solid form, preparing it for excretion. (Camilleri *et al.*, 2017)

Additionally, the colon compacts undigested residues into feces, aided by the activity of gut microbiota that ferment residual carbohydrates and produce short-chain fatty acids. The colon also serves as a temporary storage site for feces, allowing controlled and socially appropriate defecation through coordination with the rectum and anal sphincters. Furthermore, the mucosa contains lymphoid tissue for immune defense and goblet cells that produce mucus to lubricate feces and protect the intestinal lining. Overall, the large intestine is essential not only for water and electrolyte balance and fecal formation but also for maintaining continence and supporting mucosal immunity, highlighting its critical role in gastrointestinal health. (Camilleri *et al.*, 2017)

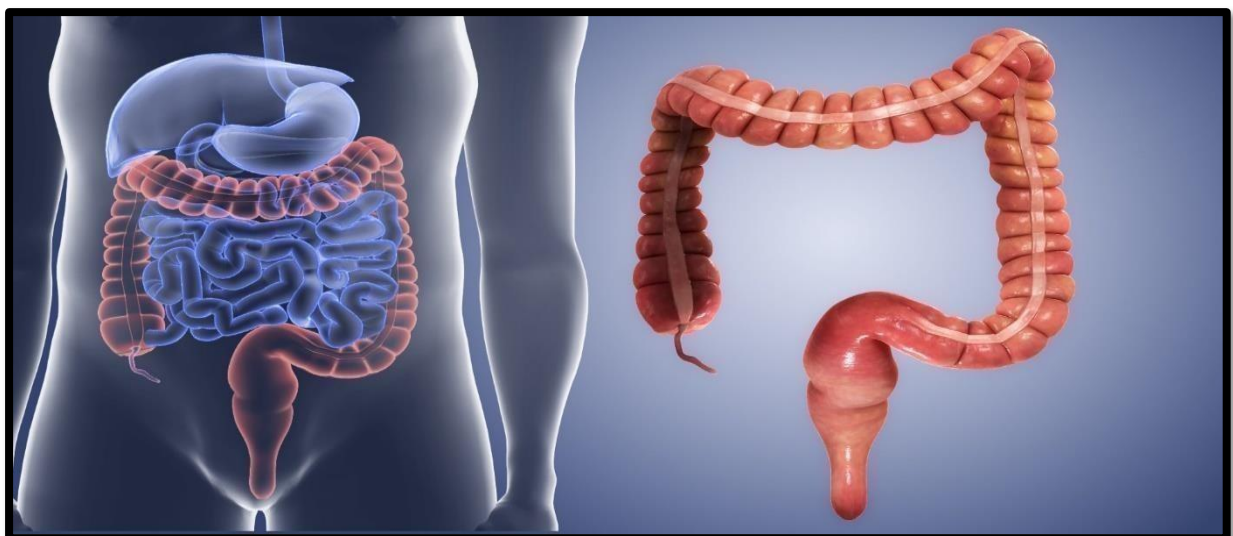


Figure 1: General location of the large intestine (Khera, 2019).

1.1. The Colon (Anatomical Segments)

The colon, forming the major portion of the large intestine, is anatomically subdivided into segments that frame the loops of the small intestine. (Kamina, 2014)

Each segment has distinct anatomical features, relations, and functions:

❖ The Cecum:

- **Location:** The cecum is the initial segment of the colon, located in the right iliac fossa, just below the ileocecal junction. (Kamina, 2014)
- **Structure:** It is a blind-ended pouch, approximately 6–7 cm in length. (Kamina, 2014)
- **Function:** Receives chyme from the ileum and initiates the process of water and electrolyte absorption. (Kamina, 2014)
- **Appendix:** The vermiform appendix arises from the posteromedial wall of the cecum; it is a narrow tubular structure with lymphoid tissue, contributing to immune defense. (Kamina, 2014)

❖ The Ascending Colon (Right Colon):

- **Course:** Extends vertically along the right lateral abdominal wall, from the cecum up to the right colic (hepatic) flexure beneath the liver. (Kamina, 2014)
- **Relations:**
 - Anteriorly: Partially covered by the peritoneum.
 - Posteriorly: Lies against the posterior abdominal wall, including the iliacus and quadratus lumborum muscles. (Kamina, 2014)
- **Function:** Absorbs water and electrolytes, forming semisolid feces; propels contents superiorly toward the transverse colon. (Kamina, 2014)

❖ The Transverse Colon:

- **Course:** The longest and most mobile segment of the colon; crosses the abdomen horizontally from the hepatic flexure on the right to the splenic flexure on the left. (Kamina, 2014)
- **Mesocolon:** Attached to the posterior abdominal wall by the transverse mesocolon, allowing some mobility and preventing kinking. (Kamina, 2014)
- **Relations:**
 - Anteriorly: Covered by the greater omentum.
 - Posteriorly: Related to the pancreas and small intestine loops. (Kamina, 2014)

- **Function:** Continues absorption, particularly of water and some vitamins produced by gut microbiota; also allows fermentation of undigested residues. (Kamina, 2014)

❖ **The Descending Colon (Left Colon):**

- **Course:** Runs vertically down the left side of the abdomen, from the splenic flexure to the sigmoid colon in the left iliac fossa. (Kamina, 2014)
- **Relations:**
 - Posteriorly: Retroperitoneal, lying against the posterior abdominal wall.
 - Anteriorly: Covered partially by the peritoneum. (Kamina, 2014)
- **Function:** Stores formed fecal material and regulates its movement toward the sigmoid colon. (Kamina, 2014)

❖ **The Sigmoid Colon:**

- **Course:** S-shaped terminal portion of the colon located in the left iliac fossa, connecting the descending colon to the rectum. (Kamina, 2014)
- **Mesocolon:** Suspended by the sigmoid mesocolon, allowing some mobility. (Kamina, 2014)
- **Function:** Acts as a fecal reservoir, regulating transit to the rectum and facilitating voluntary defecation. (Kamina, 2014)
- **Clinical Note:** Its S-shape and mobility make it a common site for diverticulosis and volvulus. (Kamina, 2014)

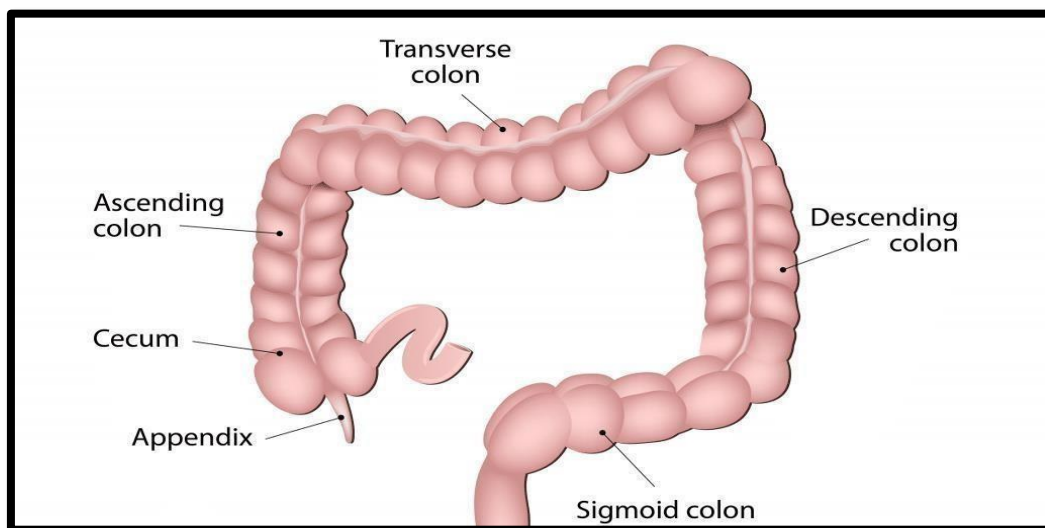


Figure 2: Anatomical components of the colon (Camilleri *et al.*, 2017).

1.2. The Rectum

The rectum is the fixed terminal segment of the digestive tract, connecting the sigmoid colon to the anal canal. Its structure and positioning are highly specialized to ensure fecal storage, continence, and controlled defecation. (Kenhub, 2024)

❖ General Features

- **Length:** Approximately 12–16 cm, measured from the end of the sigmoid colon to the anal canal. (Kenhub, 2024)
- **Position:** It follows the sigmoid colon at the level of the 3rd sacral vertebra (S3). (Kenhub, 2024)
- **Function:** Serves as a temporary storage site for fecal material and participates in the defecation reflex. (Kenhub, 2024)

❖ Location:

- **Pelvic position:** Located within the lesser pelvis, in front of the sacrum and coccyx. (Kenhub, 2024)

❖ Relation to surrounding structures:

- **Anteriorly:** In males, related to the prostate and bladder; in females, related to the vagina and uterus. (Kenhub, 2024)
- **Posteriorly:** Lies against the sacrum and coccyx. (Kenhub, 2024)
- **Laterally:** Bounded by the levator ani muscles and endopelvic fascia. (Kenhub, 2024)

This fixed position ensures stability during fecal storage and defecation. (Kenhub, 2024)

❖ Morphology:

▪ Rectal ampulla:

- ❖ The rectum has a dilated portion in its mid-lower segment, called the ampulla of the rectum.
- ❖ The ampulla functions as a reservoir, allowing temporary storage of feces.
- ❖ Distension of the ampulla by fecal matter activates stretch receptors, triggering the defecation reflex, coordinated via autonomic and somatic nervous inputs. (Kenhub, 2024)

▪ Curvature:

The rectum is slightly curved following the concavity of the sacrum (sacral flexure) and then curves anteriorly toward the anal canal (anorectal flexure), which helps maintain continence. (Kenhub, 2024)

▪ Peritonealization:

The relationship of the rectum to the peritoneum varies along its length:

- **Upper third:** Partially intraperitoneal, covered anteriorly and laterally by the peritoneum. (Kenhub, 2024)
- **Middle third:** Retroperitoneal/subperitoneal on its posterior and lateral surfaces. (Kenhub, 2024)
- **Lower third:** Subperitoneal, completely surrounded by mesorectum (fatty connective tissue containing blood vessels, lymphatics, and nerves). (Kenhub, 2024)

❖ This anatomical arrangement:

- Provides support and cushioning for the rectum.
- Protects vascular and lymphatic structures within the mesorectum.
- Is important for surgical procedures like total mesorectal excision in rectal cancer.. (Kenhub, 2024)

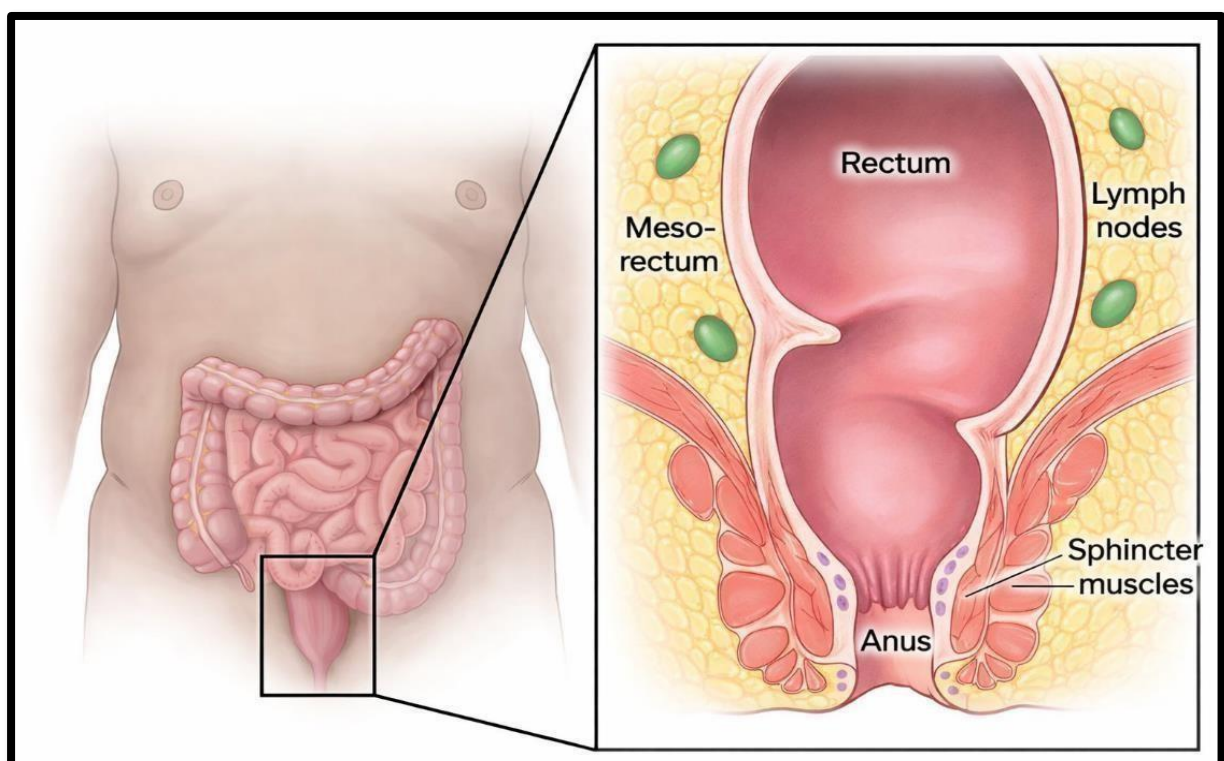


Figure 3: Anatomical view of the rectum (Netter, 2019).

2. Histology and Physiology

2.1 Wall structure (Histology)

The colonic and rectal wall is composed of four main tunics (layers) arranged from the lumen toward the outer surface. Each layer has a distinct structure and function critical for digestion, absorption, motility, and immune defense. (Kenhub,2024)

2.2. The Mucosa:

❖ Structure:

- **Epithelium:** Simple columnar epithelium specialized for absorption and secretion. (Kenhub, 2024)
- **Crypts of Lieberkühn:** Invaginations of the mucosa into the lamina propria; contain stem cells, goblet cells, and enterocytes. (Kenhub, 2024)
- **Goblet cells:** Highly abundant; secrete mucus that lubricates feces and facilitates intestinal transit. (Kenhub, 2024)
- **Lamina propria:** Loose connective tissue housing lymphoid follicles, blood vessels, and immune cells, providing local immune defense. (Kenhub, 2024)
- **Muscularis mucosae:** Thin layer of smooth muscle fibers beneath lamina propria; allows local movements of the mucosa to enhance absorption. (Kenhub, 2024)

❖ Function:

- Facilitates absorption of water, electrolytes, and nutrients.
- Produces mucus for smooth passage of stool.
- Provides immunological protection via lymphoid follicles (GALT – gut-associated lymphoid tissue). (Kenhub, 2024)

2.3. The Submucosa:

❖ Structure:

- Comprised of dense, irregular connective tissue supporting the mucosa.
- Contains blood vessels and lymphatic vessels for nutrient transport and immune surveillance.
- Contains Meissner's (submucosal) nerve plexus, part of the enteric nervous system, regulating local secretions and blood flow. (Kenhub,2024)

❖ Function:

- Provides structural support for mucosa.
- Acts as a conduit for vessels and nerves.
- Facilitates coordination of local motility and secretion. (Kenhub, 2024)

2.4. The Muscularis:**❖ Structure:** Two smooth muscle layers:

- a. **Inner circular layer:** Encircles the lumen; contracts to mix contents and propel feces forward. (Kenhub, 2024)
- b. **Outer longitudinal layer:** Runs along the colon; in the colon, forms three distinct bands (taeniae coli), which create haustra (pouches of the colon). (Kenhub, 2024)
 - In the rectum, longitudinal layer becomes continuous, without taeniae coli.
 - Auerbach's (myenteric) plexus lies between the circular and longitudinal layers, controlling peristalsis. (Kenhub, 2024)

❖ Function:

- Generates propulsive movements (peristalsis).
- Maintains colonic tone.
- Facilitates mixing of luminal contents to enhance absorption. (Kenhub, 2024)

2.5. The Serosa (or Adventitia):**❖ Structure:**

- **Serosa:** Thin layer of peritoneum covering mobile segments of the colon (e.g., transverse and sigmoid colon). (Kenhub, 2024)
- **Adventitia:** Dense fibrous connective tissue covering fixed segments (e.g., ascending and descending colon, rectum). (Kenhub, 2024)

❖ Function:

- Provides structural support and attachment to surrounding tissues.
- Reduces friction for mobile segments within the peritoneal cavity. (Kenhub, 2024)

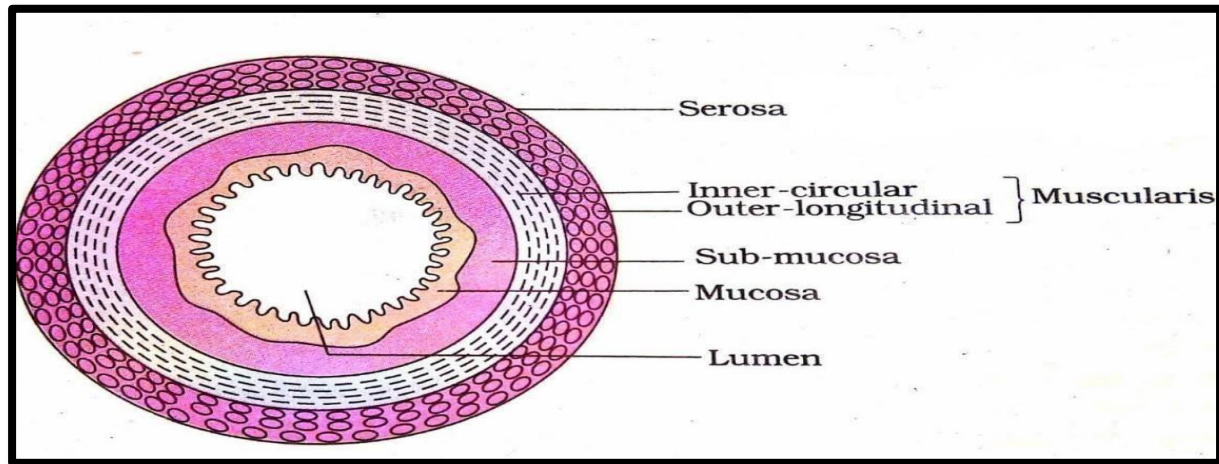


Figure 4: Histological structure of the intestinal wall (cross-section) (Ross & Pawlina ,2020).

❖ Vascularization

The colorectal complex receives a rich blood supply from two primary arterial axes: the superior mesenteric artery (SMA) and the inferior mesenteric artery (IMA). Proper vascularization is essential for nutrient delivery, tissue viability, and healing after surgery. Two main axes ensure arterial vascularization: (Moore *et al.*, 2023)

❖ The superior mesenteric artery:(SMA)

- **Origin:** The SMA arises from the anterior surface of the abdominal aorta just below the celiac trunk, typically at the level of L1 vertebra. (Moore *et al.*, 2023)
- **Distribution:** It supplies the right side of the colon, including:
 - **Cecum:** the initial pouch of the large intestine. (Moore *et al.*, 2023)
 - **Ascending colon:** extends upward from the cecum to the hepatic flexure. (Moore *et al.*, 2023)
 - **Proximal two-thirds of the transverse colon:** from the hepatic flexure to approximately the mid-transverse colon. (Moore *et al.*, 2023)
- **Branches and Collateral Circulation:**
 - **Ileocolic artery:** supplies cecum, appendix, and lower ascending colon.
 - **Right colic artery:** supplies ascending colon.
 - **Middle colic artery:** supplies proximal two-thirds of the transverse colon. (Moore *et al.*, 2023)

❖ Clinical significance:

- ✓ SMA ischemia can cause right-sided colonic infarction, particularly in elderly patients with atherosclerosis.

- ✓ SMA is crucial in surgical resections; knowledge of its branches ensures adequate blood supply to anastomose (Moore *et al.*, 2023)
- **The inferior mesenteric artery: (IMA)**
 - **Origin:** The IMA arises from the anterior aspect of the abdominal aorta at approximately L3 vertebral level, below the SMA. (Moore *et al.*, 2023)
 - **Distribution:** It supplies the left side of the colon and part of the rectum. (Moore *et al.*, 2023)
 - **Distal one-third of transverse colon:** from mid-transverse colon to splenic flexure. (Moore *et al.*, 2023)
 - **Descending colon:** extending from splenic flexure to the sigmoid colon. (Moore *et al.*, 2023)
 - **Sigmoid colon:** curves toward the pelvis. (Moore *et al.*, 2023)
 - Upper part of the rectum via the superior rectal artery. (Moore *et al.*, 2023)
 - **Branches and Collateral Circulation:**
 - **Left colic artery:** supplies descending colon and splenic flexure.
 - **Sigmoid arteries:** supply sigmoid colon.
 - **Superior rectal artery:** continuation of IMA, supplies upper rectum. (Moore *et al.*, 2023)
- ❖ **Collateral networks:**
 - a. The marginal artery of Drummond runs along the colon's inner border, connecting SMA and IMA territories, providing collateral circulation in case of arterial obstruction.
 - b. The arc of Riolan is another anastomotic connection between middle colic (SMA) and left colic (IMA), important in surgical planning and ischemia prevention. (Moore *et al.*, 2023)

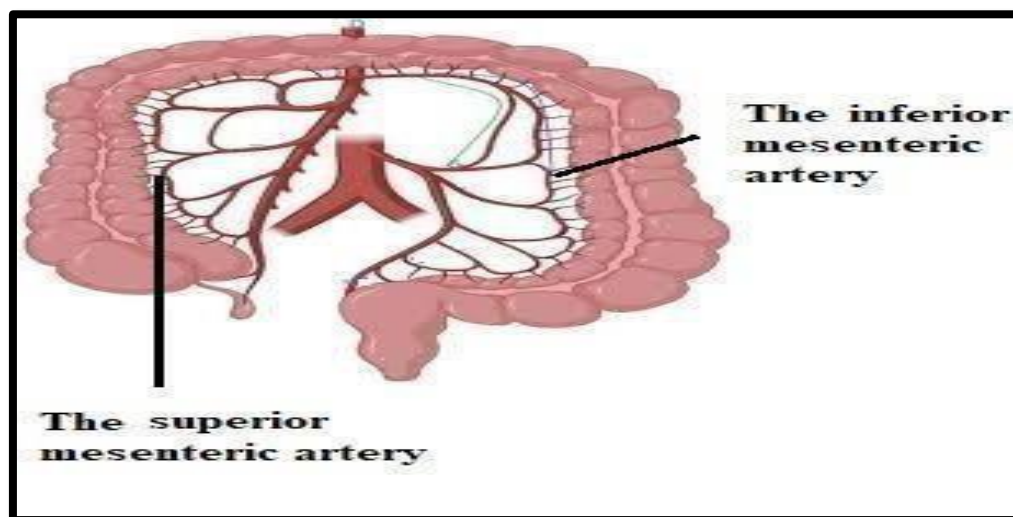


Figure 5: Diagram of the superior and inferior mesenteric arteries of the colon. (Teach, 2024)

3. Physiological Functions

The colorectal complex, which includes the colon and rectum, is a key component of the digestive tract. Its physiological roles can be divided into three main functions. (Favro ,2023)

3.1 Absorption:

The colon is responsible for absorbing water and electrolytes from the chyme that enters from the small intestine.

On average, about 1.5 liters of fluid are processed daily, and the colon reduces it to approximately 150 grams of solid stool.

This process helps maintain the body's fluid and electrolyte balance.

Sodium (Na^+), potassium (K^+), and chloride (Cl^-) ions are absorbed actively, and water follows passively via osmosis.

Without proper colonic absorption, patients may experience diarrhea or dehydration (Favro,2023)

3.2. Fermentation:

The colon contains a dense and diverse gut microbiota, including bacteria such as Bacteroides, Firmicutes, and Lactobacillus. (Favro, 2023)

These microbes ferment undigested carbohydrates and fibers, producing:

- Short-chain fattyacids (SCFAs) like acetate, propionate, and butyrate, which serve as an energy source for colonocytes. (Favro, 2023)
- Gases such as hydrogen, methane, and carbon dioxide. (Favro, 2023)

Fermentation also contributes to vitamin synthesis, including vitamin K and some B vitamins, which are absorbed in the colon. (Favro, 2023)

This activity is essential for maintaining gut health and metabolic balance. (Favro, 2023)

4. Continence and Defecation:

The rectum acts as a temporary storage reservoir for stool. This function is known as continence, allowing controlled accumulation of feces. (Favro, 2023)

Sphincter mechanisms regulate the timing of defecation:

- Internal anal sphincter: involuntary, smooth muscle; maintains baseline tone to prevent leakage. (Favro, 2023)
- External anal sphincter: voluntary, skeletal muscle; allows conscious control of defecation. (Favro, 2023)

Recto anal inhibitory reflex: When the rectum fills, the internal sphincter relaxes, signaling the need to defecate. (Favro, 2023)

These mechanisms ensure voluntary and socially acceptable defecation, protecting continence (Favro, 2023).

Chapter II

colorectal cancer

1. Definition

Colorectal cancer encompasses both colon and rectal cancers, as it can arise in either part of the large intestine. This disease develops when the normal regulation of cell growth is disrupted, leading to abnormal proliferation of epithelial cells, which cluster together to form a cancerous tumor that can invade surrounding tissues and, in advanced stages, metastasize to distant organs such as the liver and lungs. Understanding colorectal cancer requires knowledge of the anatomical and functional differences between the colon and rectum (American Cancer Society, 2023).

- 1.1. **Colon:** Commonly referred to as the large intestine, the colon is the final segment of the digestive system responsible for absorbing water and electrolytes, compacting undigested residues into feces, and temporarily storing them before passage to the rectum. Colon cancers account for nearly 60% of all colorectal cancers. Tumors can develop in any part of the colon, including the proximal colon (cecum and ascending colon), the transverse colon, or the distal colon (descending and sigmoid colon). The location influences the clinical presentation: right-sided tumors often present with anemia or occult bleeding, whereas left-sided tumors more commonly cause changes in bowel habits, obstruction, or visible blood in stool. (National Cancer Institute (NCI), 2023)
- 1.2. **Rectum:** rectum is the terminal portion of the large intestine, connecting the sigmoid colon to the anal canal. Its primary role is temporary fecal storage and coordination of voluntary defecation. Nearly 40% of colorectal cancers involve the rectum, most frequently the sigmoid portion, which is anatomically predisposed due to its S-shaped curvature and mobility . Rectal tumors may present with rectal bleeding, tenesmus (a feeling of incomplete evacuation), or changes in stool caliber, and their management often requires consideration of surgical accessibility and preservation of continence. (National Cancer Institute, 2023)

The appearance of colorectal cancer reflects the underlying cellular pathology: normal epithelial cells undergo genetic and epigenetic alterations, losing normal growth control, proliferating excessively, and forming clusters that aggregate into a malignant tumor mass . These changes disrupt normal intestinal function and, if untreated, can lead to local invasion, obstruction, or distant metastasis. Early detection, screening, and understanding of the colon and rectum's anatomy are therefore critical for effective diagnosis and treatment.(Kumar *et al.*, 2020)

2. Pathophysiology of CRC (Pathogenesis)

Colorectal cancer (CRC) typically develops over a long period of 10 to 15 years, during which the normal intestinal epithelium undergoes gradual molecular and cellular changes, eventually leading to the formation of a malignant lesion. These changes include the accumulation of genetic mutations and epigenetic alterations, which disrupt normal cell cycle regulation, apoptosis, and DNA repair mechanisms. (HAS, 2024)

2.1. The progression from adenoma to carcinoma

Between 60% and 80% of colorectal cancers arise from pre-existing benign polyps, highlighting the importance of adenoma detection and removal in CRC prevention (INCa, 2025). The adenoma-to-carcinoma sequence involves several steps:

2.2. Polypus adenoma (Adenomatous polyp):

This is the most common type of colorectal polyp and represents the initial stage of the adenoma-carcinoma sequence. (SNFGE, 2024)

- **Histology:** Composed of dysplastic epithelial cells that proliferate in a glandular pattern, sometimes forming tubular, villous, or tubulovillous structures. (SNFGE, 2024)
- **Malignant Potential:** Although most adenomatous polyps do not progress to cancer (only about 1 in 100), the risk of transformation increases significantly with polyp size. Polyps larger than 1 cm in diameter carry a 1 in 10 risk of developing malignancy. (SNFGE, 2024)
- **Clinical Relevance:** Early detection through colonoscopy and polypectomy can prevent progression to CRC, making screening programs highly effective. (SNFGE, 2024)

2.3. Serrated polyp:

Serrated polyps represent an alternative pathway to colorectal carcinogenesis, distinct from the traditional adenoma-carcinoma sequence. (Rex *et al.*, 2012)

- **Molecular Mechanisms:** They often involve specific genetic and epigenetic alterations, including DNA methylation, microsatellite instability (MSI), and BRAF mutations, which contribute to abnormal cell proliferation and malignant transformation. (Rex *et al.*, 2012)
- **Types:** This group includes hyperplastic polyps, sessile serrated adenomas, and traditional serrated adenomas, with sessile serrated adenomas being particularly prone to progression if left untreated. (Rex *et al.*, 2012)

- **Clinical Importance:** Serrated lesions are often flat and difficult to detect endoscopically, making them a subtle but significant risk factor for CRC. (Rex *et al.*, 2012)

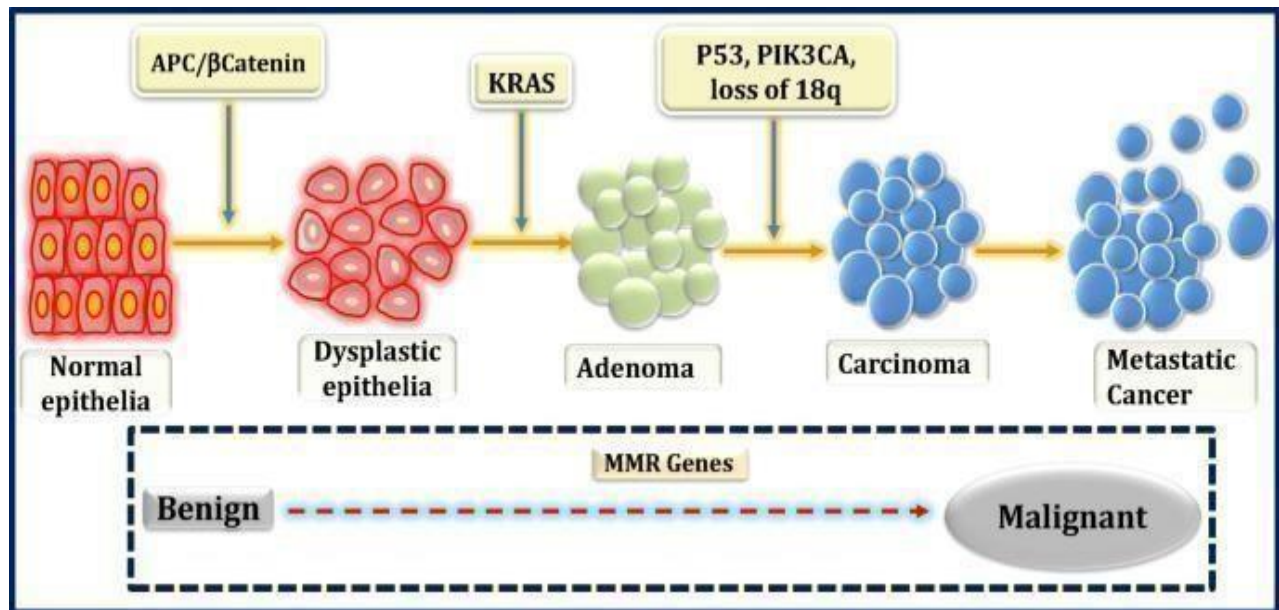


Figure 6: Integrated model of colorectal cancer progression (Fearon et Vogelstein, 1990).

(A) Histological changes from normal mucosa to metastasis; (B) Acquired genetic alterations in adenomatous and serrated pathways; (C) Comparative timeline for screening tests. (Balchan *et al.*, 2016)

3. Molecular and Genetic Mechanisms

Colorectal cancer (CRC) develops because of the accumulation of genetic and epigenetic alterations that progressively disrupt the normal regulation of the cell cycle, apoptosis, and DNA repair. These changes enable epithelial cells to proliferate uncontrollably, evade programmed cell death, and acquire invasive and metastatic potential (Fearon & Vogelstein, 1990). The main molecular pathways involved in CRC pathogenesis include:

3.1 Chromosomal instability (CIN) is characterized by numerical and structural alterations of chromosomes, resulting in the loss or gain of large chromosomal segments. This pathway involves mutations in tumor suppressor genes, such as APC and TP53, along with activation of oncogenes like KRAS, which sequentially drive the progression from normal epithelium to adenoma and ultimately to carcinoma. CIN represents the most common molecular pathway in colorectal cancer, occurring in approximately 85% of cases. Clinically, tumors

arising through CIN often display chromosomal gains or losses and aneuploidy, and they may exhibit different responses to chemotherapy compared to other molecular subtypes (Fearon & Vogelstein, 1990; Pino & Chung, 2010).

3.2. Microsatellite instability (MSI pathway): Microsatellite instability (MSI) arises from defective DNA mismatch repair (MMR) mechanisms, leading to the accumulation of errors in repetitive DNA sequences known as microsatellites. MSI is commonly associated with loss of function in MMR genes, including MLH1, MSH2, MSH6, and PMS2. Clinically, MSI is a hallmark of Lynch syndrome, a hereditary colorectal cancer syndrome, but it can also occur sporadically due to epigenetic silencing of MMR genes. Tumors with high levels of MSI (MSI-high) generally have a better prognosis and may respond differently to immunotherapy compared to tumors arising through the chromosomal instability pathway (Boland & Goel, 2010).

3.3. CIMP Methylation Phenotype: CpG Island Methylator Phenotype (CIMP) is characterized by hypermethylation of CpG islands in the promoter regions of tumor suppressor genes, resulting in their silencing. This epigenetic pathway is frequently associated with serrated polyps and mutations in BRAF, representing an alternative mechanism of colorectal carcinogenesis. Clinically, CIMP-positive tumors display distinct histological and molecular features, and identifying them is important for risk stratification and guiding personalized therapeutic approaches (Weisenberger *et al.*, 2006).

4. Stages of Carcinogenesis

The process of colorectal carcinogenesis is a multistep biological event that involves the accumulation of genetic and epigenetic alterations, ultimately transforming a normal colonic epithelial cell into an invasive and metastatic cancer cell. According to the classical model described by Fearon and Vogelstein (1990), this progression can be divided into four essential stages:

4.1. Triggering: The carcinogenic process in the colon begins with a genetic alteration in a single stem cell located at the base of a colonic crypt. This initial mutation commonly affects key tumor suppressor genes or oncogenes, such as APC, disrupting the normal regulation of cell proliferation and differentiation. As a result, the single mutated stem cell can act as the initiator of colorectal tumorigenesis, providing a foundation for subsequent

clonal expansion and the development of adenomas and eventually carcinomas. (Barker *et al.*, 2009)

- 4.2. **Promotion:** During this stage, the mutated cell starts to proliferate, giving rise to a clone of cells that evades normal growth control mechanisms. This uncontrolled proliferation results in the formation of a polyp, which may be either adenomatous or serrated, depending on the specific pathway of carcinogenesis involved. Clinically, these polyps are significant because they represent precancerous lesions that can be detected and removed, thereby interrupting the progression toward invasive colorectal cancer (Fearon & Vogelstein, 1990).
- 4.3. **Evolution:** During this stage, successive genetic and epigenetic alterations accumulate within the polyp, progressively enhancing its malignant potential. Mutations in additional tumor suppressor genes, such as TP53, and oncogenes, like KRAS, drive the transformation of the benign polyp into a malignant tumor. As a result, the tumor gains the capacity to invade the submucosa or muscularis propria, marking the critical transition from a localized precancerous lesion to an invasive carcinoma (Fearon & Vogelstein, 1990).
- 4.4. **Spread:** In the final stage of colorectal carcinogenesis, cancer cells acquire the ability to invade blood and lymphatic vessels, allowing them to spread to distant sites. The liver is the most common site of metastasis due to the portal venous drainage from the colon, while other potential targets include the lungs, peritoneum, and regional lymph nodes. Clinically, this capacity for dissemination signifies the transition from a potentially curable localized disease to advanced, life-threatening cancer, highlighting the critical importance of early detection and timely intervention (Chambers *et al.*, 2002).

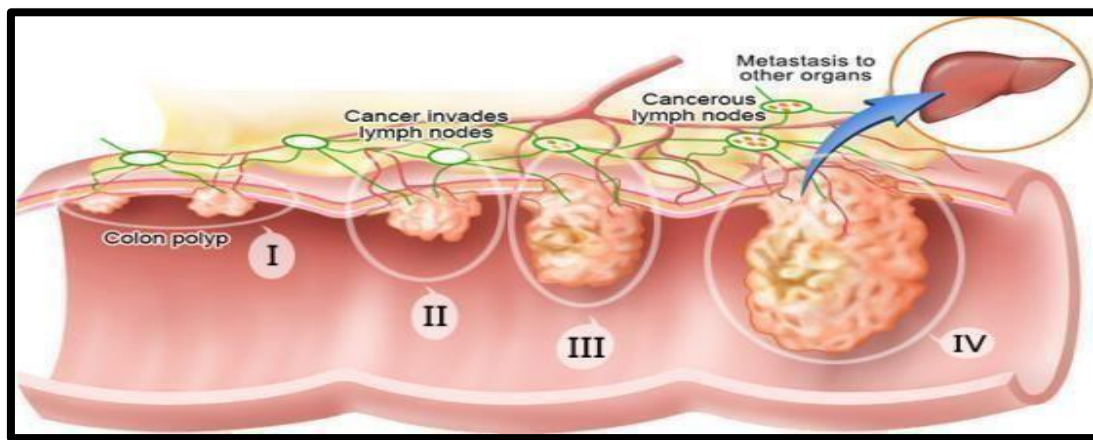


Figure 7: Stages of Colorectal Cancer (CRC) progression (American Cancer Society, 2024).

(I) Localized colon polyp; (II) Invasion of the colonic wall; (III) Invasion of regional lymph nodes; (IV) Distant metastasis to the liver and other organs. (National Cancer Institute, 2024).

5. Risk Factors for colorectal cancer :

The development of colorectal cancer (CRC) is not determined solely by genetic predisposition but is also strongly influenced by environmental and lifestyle factors that affect the colonic environment. These factors can promote chronic inflammation, cellular damage, and accumulation of mutations, thereby increasing the risk of malignant transformation (Keum & Giovannucci, 2019). The main risk factors include:

5.1. Non-modifiable factor

Colorectal cancer is one of the deadliest cancers worldwide and represents a major public health challenge. According to 2022 figures from the International Agency for Research on Cancer (IARC) in Algeria, 7,747 new cases were reported, while the disease accounted for 4,380 deaths. It is the second most common cancer in the country, just behind breast cancer, and affects both men and women. This high prevalence, coupled with a significant mortality rate, highlights the need for early screening and preventive measures to reduce the burden of this disease in Algeria. (CIRC, 2022)

5.1.1. Age:

Although colorectal cancer predominantly affects individuals over the age of 50, recent years have shown a concerning rise in the number of cases among younger populations. This emerging trend is particularly alarming, as it may reflect changes in lifestyle, environmental exposures, or genetic predispositions. Typically, the average age at diagnosis ranges between 50 and 60 years, which corresponds to the period when the risk of developing the disease

significantly increases. However, the growing incidence among younger individuals highlights the need for increased awareness, earlier screening strategies, and a better understanding of potential risk factors contributing to this shift. (World Health Organization, 2023; International Agency for Research on Cancer, 2020)

5.1. .2. Sex:

Colorectal cancer affects both men and women, although it appears to be more common in men. In 2022, 4,082 men were diagnosed with the disease compared to 3,665 women. This difference may be due to several factors, including lifestyle, such as diet, smoking, and physical activity, as well as differences in participation rates in screening programs. Despite this disparity, the disease remains widespread in both sexes, demonstrating that colorectal cancer is a major public health problem. (CIRC, 2022)

5.2. Genetic and hereditary factors :

Two hereditary forms of colorectal cancer exist:

5.2.1. Familial adenomatous polyposis (FAP)

is a rare hereditary condition that accounts for approximately 1% of colorectal cancers. It is caused by a mutation in the APC tumor suppressor gene, which plays a key role in regulating cell proliferation. This condition is characterized by the appearance, beginning in adolescence, of numerous polyps in the colon and rectum, which are easily identifiable during a colonoscopy and whose number gradually increases with age. Due to the very high risk of malignant transformation, affected individuals should undergo regular medical monitoring starting at age 12. Early intervention, generally recommended starting at age 20, is essential to prevent progression to colorectal cancer. Without preventive treatment, colorectal cancer typically develops between the ages of 35 and 40. (Yen T *et al.*, 2022)

5.2.2. Lynch syndrome

Also known as hereditary non-polyposis colorectal cancer, is a genetic disorder linked to defects in the DNA repair mechanisms within cells. It accounts for approximately 2- 3% of colorectal cancers, making it the most common hereditary form of this disease. Unlike other forms, tumors associated with this syndrome do not exhibit obvious specific characteristics, making it more difficult to identify. Affected individuals have a high risk of developing colorectal cancer during their lifetime, estimated at between 30% -48% by age 70. Therefore,

to reduce this risk, regular endoscopic screening is recommended starting at age 20.(Yen T *et al.*, 2022)

5.2.3. Genetic factors :

Two major types of colorectal cancer are strongly influenced by genetic factors. The first is familial adenomatous polyposis, which results from a mutation in the APC gene. Lynch syndrome, also known as hereditary non-polyposis colorectal cancer (HNPCC), is associated with mutations in genes such as MSH2, MSH6, MLH1, PMS2, and EPCAM. These genes are responsible for producing proteins that play a key role in DNA repair. These hereditary forms are relatively rare, accounting for less than 5% of all colorectal cancers, and they generally occur before the age of 40. (Département Prévention Cancer Environnement, Centre Léon Bérard, 2025)

5.3. Family history

A specialist may suspect that colorectal cancer is hereditary if certain family or individual risk factors are present. This may be the case if close relatives have developed colorectal cancer before the age of 50, or if two close relatives (such as a parent, sibling, or child) have been diagnosed with the disease. Furthermore, if the patient has already had two of the following types of cancer—colorectal, endometrial, ovarian, small intestine, or ureteral—this strengthens the suspicion of a hereditary form. (Yen T *et al.*, 2022)

5.4. Chronic inflammatory bowel diseases

Chronic inflammatory bowel disease (IBD), including Crohn's disease and ulcerative colitis, causes ongoing inflammation of the digestive tract. This persistent inflammation increases the risk of developing colorectal cancer, particularly when the condition lasts for several years. For patients with Crohn's disease, the risk is two to three times higher than in the general population and increases with the duration of the disease: after 10 years of ulcerative colitis, the risk is around 2%; after 20 years, it rises to 8%; and after 30 years, it could reach as high as 18%. (Roswell Park Comprehensive Cancer Center, 2022)

5.5. Diabetes

Diabetes encompasses various metabolic disorders characterized by persistent hyperglycemia, resulting from a deficiency in insulin secretion or function, or both. There are essentially two categories: type 1 diabetes (T1D) and type 2 diabetes (T2D). Type 2 diabetes, the most common

form, is characterized by insufficient insulin secretion by the pancreatic β -cells. There is an association between T2D and an increased risk of colorectal cancer. Part of this link can be explained by hyperinsulinemia, but also by prolonged intestinal transit time, which exposes the intestinal mucosa more intensely to potentially carcinogenic agents. Elevated levels of bile acids in the intestinal lumen have also been observed in patients with diabetes, which could promote tumor development. In addition, some studies have shown a modest increase in the risk of non-Hodgkin lymphoma among individuals with diabetes. This may be associated with impaired immune function, including reduced neutrophil activity and decreased cellular and humoral immunity. In conclusion, epidemiological data show that the risk of colorectal cancer is higher in patients taking sulfonylureas or insulin. (Karmi Khaoula *et al*, 2020)

5.6. Obesity and Overweight

Obesity is a major risk factor for colorectal cancer. It increases disease risk of developing the disease by approximately 25%, with this effect being more pronounced in men. This relationship is largely influenced by metabolic syndrome, which is commonly associated with abdominal obesity. Although some research has suggested that bariatric surgery may have varying effects depending on metabolic changes and the microbiome, it reduces the risk of colorectal cancer in obese individuals. Obesity also affects prognosis and treatment: it can reduce the effectiveness of certain treatments and increase the risk of postoperative complications, such as infections. For patients with rectal cancer, a high body mass index is associated with an increased risk of local recurrence, although overall survival is not consistently affected. In summary, maintaining a healthy weight and preventing obesity is crucial for reducing risk and improving the prognosis of colorectal cancer. (Qu  n  herv   et al., 2021)

5.7. Cholecystectomy

The link between cholecystectomy that is, the surgical removal of the gallbladder and the risk of colorectal cancer remains a subject of controversy. Some studies suggest an increased risk following this procedure, while others find no significant link. This controversy stems primarily from the physiological changes caused by cholecystectomy. Indeed, without the gallbladder, bile flow is no longer intermittent but occurs continuously into the intestine. This change facilitates the conversion of primary bile acids by intestinal microorganisms into secondary bile acids. These factors can have harmful effects on the colon lining, particularly by generating free

radicals, damaging cell membranes, and causing DNA damage. These processes may therefore contribute to the development of colorectal cancer. (Bouguerne Ahlem, 2025)

5.8. An imbalance in the gut microbiota

- The gut microbiota is crucial for maintaining homeostasis in the host, primarily by contributing to the maturation of the local and systemic immune systems. An imbalance in this microbial ecosystem, known as dysbiosis, is often observed in various chronic diseases, including colorectal cancer. This suggests a possible role in colorectal carcinogenesis. (Fidelle *et al.*, 2023)
- In the case of colorectal cancer, several studies have demonstrated a significant change in the composition of the gut microbiota, both in the affected tissues and in patients' stool samples, compared to healthy individuals. This dysbiosis is characterized by an overgrowth of certain bacteria known as pathobionts, often originating in the mouth, such as *Fusobacterium nucleatum*, *Parvimonas micra*, *Peptostreptococcus stomatis*, *Peptostreptococcus anaerobius*, *Porphyromonas asaccharolytica*, *Solobacterium moorei*, and *Prevotella intermedia*. A link has been established between these species and the onset and progression of colorectal cancer, as well as precancerous lesions such as polyps.
- Similarly, a reduction in beneficial commensal bacteria is often observed in people with colorectal cancer. Genus such as *Lactobacillus*, *Streptococcus thermophilus*, *Streptococcus salivarius*, and *Clostridium butyricum* are often less abundant. This imbalance between beneficial and pathogenic bacteria contributes to an unstable intestinal environment, which is conducive to chronic inflammation and alterations in the epithelial barrier. (Fidelle *et al.*, 2023)
- It has also been observed that gut dysbiosis is associated with specific changes depending on the molecular subtypes of colorectal cancer, with bacterial overgrowth varying according to tumor profiles. Bacteria such as *Fusobacterium nucleatum* and *Bacteroides fragilis* are notably linked to more aggressive tumor types and to phenotypes associated with a compromised immune response. (Fidelle *et al.*, 2023)
- From a mechanistic perspective, various studies highlight a causal role of the microbiota in colorectal carcinogenesis. Specific pathogenic bacteria secrete toxins and genotoxic metabolites that have the ability to damage the DNA of epithelial cells, activate oncogenic pathways such as Wnt/ β -catenin, and trigger persistent inflammatory responses involving, among others, IL-17. These processes promote a pro-tumor microenvironment that facilitates the initiation and development of cancer. (Fidelle *et al.*, 2023)

- In addition, bacteria such as *Fusobacterium nucleatum* are often associated with a poorer prognosis, resistance to treatment, and an unfavorable immune response. Other toxin-producing species, such as *Escherichia coli pks+*, *enterotoxigenic Bacteroides fragilis*, or *Streptococcus gallolyticus*, also contribute to the formation of bacterial biofilms on the colonic mucosa. These biofilms, frequently observed in patients with colorectal cancer, promote bacterial invasion, the production of inflammatory mediators, and the disruption of epithelial integrity. (Fidelle *et al.*, 2023)

5.9. Dietary factors

Diet plays a central role in colorectal carcinogenesis. Many nutrients and foods may act either as risk-promoting or protective factors. However, the relationship between diet and colorectal cancer remains complex due to interactions between dietary components and variability in individual eating patterns. (Aune *et al.*, 2011)

Dietary intake can influence the development of colorectal tumors, including both adenomas and carcinomas. Nevertheless, the precise role of specific dietary factors in the progression from adenoma to carcinoma remains difficult to determine, as food components are usually consumed in combination, making it challenging to isolate their individual effects (Aune *et al.*, 2011)

Dietary factors associated with risk

5.9.1. Red and processed meats:

Evidence suggests that the consumption of red and processed meat increases the risk of colorectal cancer, and largely than overall meat consumption. By red and processed meat, we mean beef, pork, and lamb, as well as sausages, deli meats, hamburgers, and smoked, grilled, or canned meats. Several factors may be associated with this risk: heterocyclic amines that form on the surface of cooked meats, nitrosamines generated internally within the food, or even the iron present in red meat. Norat (2002) reviewed most of the research published over the past forty years and observed a moderate but significant increase in the risk of colorectal cancer. According to this study, the relative risk associated with red meat is 1.35 (1.21–1.51), while for processed meat, it is 1.31 (1.13–1.51), when comparing the highest and lowest consumption quintiles. It should be noted that, for the same weight, processed meats pose a risk three to four times higher than that of red meat. However, overall meat consumption does not show a significant association with risk (RR = 1.14 [0.99–1.31]). According to the author, between 10 and 25 percent of colorectal cancer cases may be attributable to meat consumption in areas

where meat consumption is high. Although suggestions have been made to limit daily meat consumption (Valérie Hallé, 2002)

5.9.2. Cooking fats and fried foods

- 1) **Dietary fats:** It appears that excessive consumption of fats, especially those of animal origin, increases the risk of developing colorectal cancer. (World Cancer Research Fund / American Institute for Cancer Research, 2018)
- 2) **Animal fats:** Excessive consumption of red meat (such as beef, pork, and lamb) and processed meats stimulates the production of bile acids in the intestine. Some of their metabolic byproducts have a direct cytotoxic effect on the colonic mucosa, thereby contributing to cellular instability. (O’Keefe, 2016)
- 3) **Tran’s fatty acids:** Derived primarily from industrial processing, they are linked to an increased risk of cancer by promoting chronic systemic inflammation. (Anses, 2011)
- 4) **Vegetable oils:** An excess of omega-6 fatty acids (found in sunflower or corn oils), not balanced by sufficient intake of omega-3s, could create a biochemical environment conducive to tumor growth. (Anses, 2011)

5.9.3. Frying and cooking methods

Frying alters the chemical structure of foods and oils, which can lead to the formation of potentially carcinogenic compounds. (EFSA, 2015)

- 1) **Formation of genotoxic substances:** During high-temperature cooking, particularly frying, heterocyclic amines, (HCAs) and polycyclic aromatic hydrocarbons (PAHs) are generated through the breakdown of proteins and fats. These compounds are known for their ability to directly damage the DNA of cells in the colon lining. (Cross & Sinha, 2004)
- 2) **Acrylamide detected:** This compound, considered a possible carcinogen, is produced during the Maillard reaction when starchy foods such as potatoes are fried. Health authorities closely monitor the regular consumption of these products. (Cross & Sinha, 2004)
- 3) **Promotion of inflammation:** Eating fried foods, which are high in fats oxidized during cooking, stimulates inflammation in the digestive system. This persistent inflammation promotes polyp formation and tumor progression (Cross & Sinha, 2004).

5.9.4. Highly processed foods

Several studies have reported a growing association between colorectal cancer and nutritional factors, particularly the consumption of highly processed foods. Numerous studies, particularly

those conducted by the International Agency for Research on Cancer and the NutriNet-Santé cohort, have demonstrated a link between these products and an increased risk of cancer. According to the NOVA classification, ultra-processed foods are characterized by their high content of added sugars, salt, fats, and additives such as emulsifiers. These substances have the potential to disrupt the balance of gut flora and promote persistent inflammation. Epidemiological data also suggest a link between the consumption of emulsifiers and certain types of cancer. Furthermore, recent research suggests that these foods promote colorectal cancer development by triggering long-term inflammatory processes, characterized by elevated levels of pro-inflammatory substances and reduced levels of anti-inflammatory agents, such as resolvins derived from omega-3 fatty acids. Consequently, adopting a diet rich in unprocessed foods and essential fatty acids could reduce chronic inflammation and have a preventive effect against the onset and progression of colorectal cancer. (Julie P., 2025)

5.9.5 Alcohol and sugary drinks

- 1) **Alcohol Consumption** Alcohol poses a significant risk for the development of colorectal cancer. According to various epidemiological studies, daily consumption of two to three alcoholic drinks is associated with an approximate 20% increase in the risk of developing this disease. For individuals who drink more than three drinks per day, this risk can rise to nearly 40%. The risk of colorectal cancer can increase by up to 52% in people who regularly drink four or more alcoholic drinks per day, further increases the risk (Kasmi & Boulakhrouf, 2025).
- 2) **Consumption of sugary drinks:** Recent research suggests a link between the consumption of sugary drinks and the progression of colorectal cancer, particularly with regard to its ability to spread. Research conducted at the MD Anderson Cancer Center has shown that simple sugars, particularly the glucose-fructose mixture found in sodas and other sugary drinks, may promote the dissemination of cancer cells to distant organs such as the liver, regardless of weight gain or tumor size. This is due to the stimulation of cellular processes associated with energy production, which amplifies the invasive capacity of cancer cells.

Furthermore, experimental studies conducted on animal models have shown a significant increase in liver metastases in individuals fed a diet rich in these sugars. This mechanism is believed to be facilitated in particular by the activation of the enzyme sorbitol dehydrogenase (SORD), which plays a crucial role in regulating energy metabolism and stimulating glycolysis, thereby contributing to cell motility. These findings should be viewed in the context of the global rise in consumption of sugary drinks since the 1980s, which coincides with an increase

In cases of colorectal cancer among young adults. Consequently, reducing consumption of these beverages could represent a crucial preventive measure to curb the growth and spread of this cancer. (Deve, 2025)

5.10. Environmental and lifestyle factors

a) Environmental pollution

Numerous studies indicate that prolonged exposure to harmful environmental substances (such as pesticides, heavy metals, nitrates, and other contaminants) increases the risk of developing colorectal cancer (CRC). Industrial activities generate heavy metals such as mercury, lead, and cadmium, which contribute to oxidative stress and chronic inflammation, factors linked to carcinogenesis. Similarly, persistent organic pollutants (POPs), including certain pesticides found in water, are associated with an increased risk of CRC (141). Industrialization and inadequate waste management exacerbate this exposure. Furthermore, consumption (refined products, pesticide residues) contributes to exposure, while emerging factors such as microplastics and fine particulate matter may also play a role. (Hochenauer, 2025)

b) Occupational exposure

According to a study conducted as part of the RNV3P (2001–2016), several occupational risk factors for colorectal cancer have been identified, despite the fact that it is not officially recognized as a compensable occupational disease. This study identified 182 cases, with a predominance among men. Exposure to asbestos and polycyclic aromatic hydrocarbons is often associated with the disease, particularly in the construction and metalworking industries. However, no significant link has been found with pesticides or organic solvents. A potential role for welding fumes and gases has also been mentioned, although the evidence for this remains insufficient. These findings suggest a possible association between certain occupations and colorectal cancer, warranting further studies. (Clin, 2018)

c) Active and passive smoking

The risk of colorectal cancer increases with tobacco use, and this risk rises with the duration and amount of tobacco smoked. Prolonged and heavy use can promote the development of large adenomas in the colon and rectum, which are frequently responsible for colorectal cancer. Nicotine, which is the primary addictive agent, is associated with a multitude of harmful compounds present in smoke. These compounds are found in the blood and urine of both primary and secondhand smokers and can interact with DNA and proteins, leading to genetic

mutations. The presence of chemical compounds capable of damaging DNA thus explains the harmful effects of tobacco (Mehessem, 2016).

d) Sedentary Lifestyle

Sedentary lifestyle, characterized by low levels of physical activity and limited energy expenditure, is now recognized as a significant risk factor for colorectal cancer. This lifestyle is frequently associated with gradual weight gain and excess body fat, two factors that promote the development of metabolic disorders conducive to the formation of colorectal tumors. The effects are amplified by prolonged periods of inactivity, such as spending time sitting at work or in front of screens, which appear to have a direct impact on increasing the risk of colorectal cancer, independent of other dietary or genetic factors. Consequently, reducing inactivity and encouraging a more active lifestyle is proving to be a crucial approach to preventing this disease (Kheniche *et al.*, 2020).

6. Epidemiology of CRC

6.1 Global Epidemiology

According to GLOBOCAN 2022 statistics, colorectal cancer (CRC) represents a significant global health burden, with approximately 1.9 million new diagnoses and over 900,000 deaths estimated in 2022. It ranks second among the causes of cancer death globally, exhibiting higher incidence and death rates among men and in nations with a high Human Development Index (HDI). (World Health Organization, 2024)

6.2. Global Geographic Distribution

The incidence and mortality of colorectal cancer vary considerably worldwide, with significant disparities between regions and continents. According to GLOBOCAN statistics from 2022, there were approximately 1,926,425 newly diagnosed cases of colorectal cancer and 904,019 deaths from the disease globally that year, with a higher prevalence in men than in women.

Regarding regional distribution, East Asia accounted for the largest volume of cases and deaths, with approximately 699,866 cases and 316,406 deaths in 2022, denoting a heavy health burden in this area.

It was also observed that incidence rates and the criteria used differed according to geographical areas: high rates were noted in Southern and Eastern Europe, while low-income regions such

as West Africa showed high mortality rates related to infections, reflecting major challenges in terms of diagnosis and care. (Wu *et al.*, 2025)

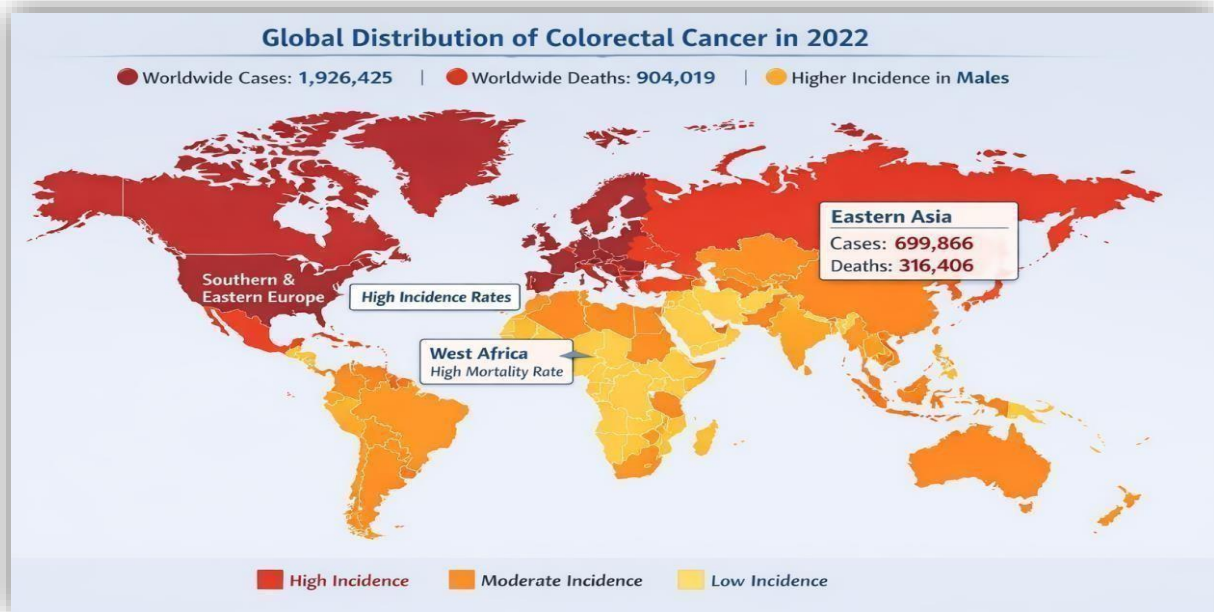


Figure 8: Mapping the global distribution of colorectal cancer in 2022 (IARC GLOBOCAN, 2022)

6.3. Epidemiology of CRC in Algeria

Colorectal cancer (CRC) is a major public health concern worldwide, with nearly 1.5 million new cases diagnosed each year. The highest incidence rates are observed in North America and Europe. In Algeria, CRC is the second most common cancer after breast cancer, with standardized incidence rates of 23 per 100,000 in men and 16 per 100,000 in women, and an estimated 2,984 deaths in 2018. Over the past decade, incidence has been rising in Algeria, whereas in France and Europe both incidence and mortality have been decreasing. Diet and lifestyle strongly influence CRC risk: high consumption of red meat, calories, and fats increases risk, while diets rich in fruits, vegetables, fish, poultry, whole grains, and regular physical activity reduce it. (Mazouzi *et al.*, 2023)

7. Histopathology of CRC

Histopathological examination of colorectal cancer (CRC) is crucial for confirming the diagnosis, determining the tumor stage, and guiding treatment decisions. It focuses on essential

parameters such as tumor differentiation, which indicates aggressiveness; depth of invasion (pT stage), which reflects disease progression; and lymph node status, a key prognostic factor requiring appropriate sampling. Additional characteristics such as venous invasion, perineural invasion, tumor perforation, and involvement of resection margins—particularly the circumferential resection margin (CRM)—provide further prognostic information and help predict the risk of recurrence. However, failure to provide a comprehensive report of these elements, particularly when using free-text formats, could lead to incorrect classification and suboptimal patient management. This is why standardization of the histopathology report is crucial. (Badmos *et al.*, 2018)

7.1 Adenocarcinomas

More than 90% of colorectal cancer cases are adenocarcinomas. Tubular adenocarcinoma, which can range from well differentiated to poorly differentiated, is the main subtype. Other subtypes include mucinous, signet-ring cell, medullary, micropapillary, spindle cell, rhabdoid, adenomatous, and low-grade tubulolobular adenocarcinomas, each with its own distinctive features and prognosis. Identifying these subtypes is crucial for diagnosis, treatment, and prognosis. (Cancer Informant, 2024)

7.2. Other forms of tumors are significantly less common

- **MALT lymphomas: lymphomas** are rare colorectal tumors that originate from mucosa-associated lymphoid tissue. They arise from immune system cells located in the colonic wall. The prognosis and treatment vary depending on the type of lymphoma; whether it is aggressive or indolent (slow growing). (Bosman *et al.*, 2019)
- **Gastrointestinal stromal tumors (GISTs)** are rare tumors (<1% of colorectal cancers) that originate in the muscles or connective tissue of the colon wall. They can be benign or malignant. Malignant forms are treated with targeted therapies, such as Glivec™. (Bosman *et al.*, 2019)
- **Carcinoid tumors** account for approximately 1% of colorectal cancers. Their clinical symptoms are primarily caused by argentaffin cells, which produce serotonin. These tumors develop slowly, typically appearing between the ages of 50 and 70, and are difficult to treat. Treatment focuses on managing acute serotonin crises. (Bosman *et al.*, 2019)

8. Colorectal Carcinogenesis Process

8.1 Adenoma–Carcinoma Sequence

A synthesis of the adenoma-carcinoma sequence has been demonstrated by selection of four spontaneous oncogenic mutations in human colon organoids deficient in mismatch repair. (Leslie *et al.*, 2002)

8.2. Phases of the adenoma-carcinoma sequence:

- a) **From normal epithelium to early adenoma:** this process is initiated by the disappearance or mutation of the APC tumor suppressor gene (Adenomatous polyposis coli (APC), which leads to hyperproliferation, usually within the Wnt signaling pathway (The Wnt signaling pathway controls cell growth and division. Normally, the APC gene prevents excessive proliferation by regulating β -catenin. When APC is mutated, β -catenin accumulates and activates genes that cause uncontrolled cell growth, leading to the formation of an early adenoma in colorectal cancer). (Vogelstein *et al.*, 1988)
- b) **From early adenoma to intermediate/late adenoma:** other mutations occur, particularly in the KRAS proto-oncogene (which stimulates cell proliferation and resists apoptosis) as well as the loss of chromosome 18q, which houses the SMAD2/4 genes. (Vogelstein *et al.*, 1988)
- c) **Transition from late adenoma to carcinoma:** Mutation or absence of the tumor suppressor gene TP53 (located on chromosome 17p) gives progressive adenomas the ability to avoid senescence, resulting in invasive cancer (Vogelstein *et al.*, 1988)
- d) **Alternative Pathway**

Although the adenoma-carcinoma pathway is the most common, another important pathway is the serrated polyp pathway (or BRAF pathway), usually identified by methylation of CpG islands and abnormalities in mismatch repair. (Kasi *et al.*, 2020)

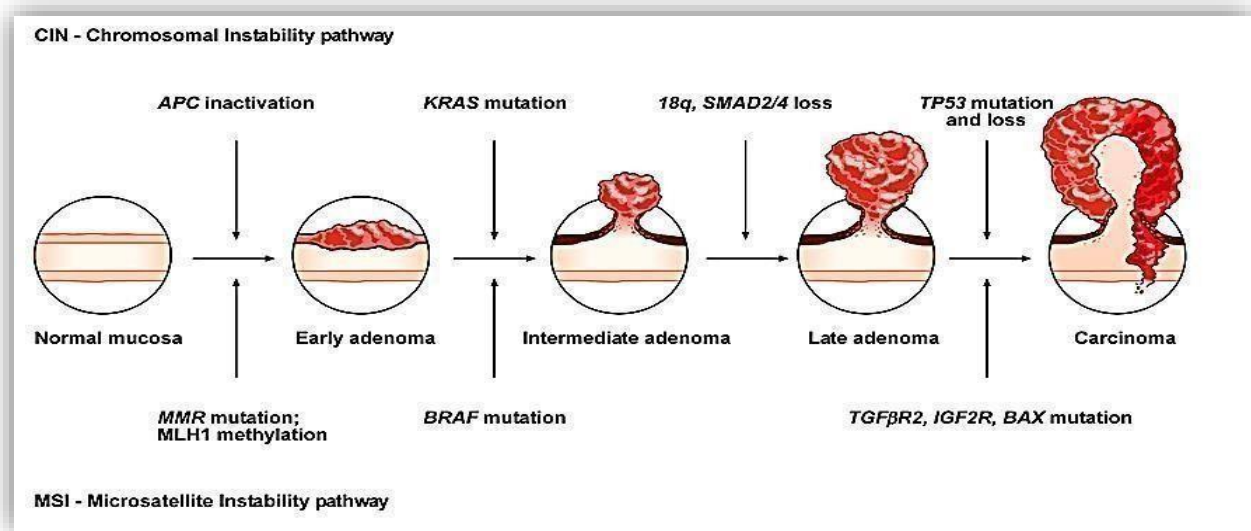


Figure 9: Molecular Progression of Colorectal Cancer: The Adenoma–Carcinoma Sequence via Chromosomal Instability (CIN) Pathway (De Palma *et al.*, 2019)

Typical sequence from adenoma to carcinoma : Chromosomal instability (CIN) begins with biallelic mutations in the tumor suppressor gene APC occurring in normal colonic mucosa. It gradually progresses to adenocarcinoma due to the appearance of additional mutations in the KRAS, SMAD4, and TP53 genes, leading to alterations in the Wnt/ β -catenin, MAPK, PI3K, and TGF- β signaling pathways. In other words, The CIN pathway involves Wnt signaling alterations, whereas the MSI pathway is related to mismatch repair deficiency., resulting in the development of a nascent adenoma. Subsequently, a mutation in the BRAF gene, followed by alterations in the TGFBR2, IGF2R, and BAX genes, contributes to progression to the intermediate and advanced stages of carcinogenesis. (De Palma *et al.*, 2019)

8.3. Genetic and epigenetic alterations

Colorectal cancer (CRC) progresses through a sequence of stages, marked by the gradual accumulation of genetic mutations (CIN/MSI) and epigenetic modifications (CIMP). These changes convert normal epithelium into carcinoma by activating oncogenes (such as KRAS) and inhibiting tumor suppressor genes (such as APC, TP53, MLH1), thereby regulating crucial behaviors such as cell proliferation and survival. (Jung *et al.*, 2020)

- **Chromosomal Instability (CIN):** Occurs in 80–85% of sporadic CRCs, leading to aneuploidy and loss of heterozygosity (e.g., chromosome 18q, APC), driving cancer initiation and progression. (Guinney *et al.*, 2024)
- **Microsatellite Instability (MSI):** A hypermutable phenotype (roughly 15% of cases) caused by defects in DNA mismatch repair (MMR) genes (e.g., MLH1, MSH2). It is often linked to epigenetic silencing of MLH1. (Cao *et al.*, 2020)
- **CpG Island Methylator Phenotype (CIMP):** Widespread promoter hypermethylation causes silencing of tumor suppressor genes and DNA repair genes (Worthley & Leggett, 2010)
- **Major Signaling Pathway Alterations:** Key driver mutations frequently affect the WNT-APC-CTNNB1 pathway, RAS-RAF-MAPK pathway, and TGFβ1-SMAD pathway (Inamura, 2018)
- **Interaction of Genetic and Epigenetic Factors**
- **Combination Mechanisms:** Many CRCs display both genetic (e.g., KRAS mutation) and multiple epigenetic alterations simultaneously. (Bardhan & Liu., 2013)
- **Environmental Impact:** Epigenetic modifications are significantly influenced by lifestyle factors (diet, smoking) and inflammation, providing a link between environmental risk and carcinogenesis. (Bardhan & Liu., 2013)
- **Clinical Relevance:** These changes create actionable targets for diagnosis and therapy (e.g. Cetuximab), with epigenetic changes being potentially reversible. (Bardhan & Liu., 2013)

9. Classification of colorectal cancer

9.1. Histological classification

The World Health Organization (WHO) primarily classifies colorectal cancer (CRC) based on cell morphology and architecture, with adenocarcinoma being the most commonly observed type. (Fleming *et al.*, 2012)

- **Mucinous Adenocarcinoma:** Defined by > 50 % of the tumor volume consisting of extracellular mucin pools. These are often associated with high-level microsatellite instability (MSI-H) and a worse prognosis if diagnosed at an advanced stage. (Dubansky *et al.*, 2024)
- **Signet Ring Cell Carcinoma:** A rare, aggressive variant where > 50 % of the tumor is composed of malignant cells containing intracellular mucin, forcing the nucleus to the periphery. (Dubansky *et al.*, 2024)

- **Medullary Carcinoma:** Characterized by solid sheets of tumor cells, frequently associated with MSI-H and better prognosis, often occurring in the right colon. (Dubansky *et al.*, 2024)
- **Serrated Adenocarcinoma:** Displays a "saw-toothed" glandular pattern, often associated with BRAF/KRAS mutations. (Dubansky *et al.*, 2024)
- **Micropapillary Carcinoma:** Defined by small clusters of tumor cells within clear spaces, often associated with high lymph node metastasis. (Dubansky *et al.*, 2024)
- **Neuroendocrine Neoplasms:** These tumors are classified separately due to their distinct neuroendocrine differentiation. (Dubansky *et al.*, 2024)
- **Other Types:** Adenosquamous carcinoma, spindle cell carcinoma, and undifferentiated carcinoma. (Dubansky *et al.*, 2024)

9.2. TNM classification

The TNM classification of colorectal tumors categorizes cancers according to T (invasion of intestinal wall), N (presence or absence of lymph node metastases), and M (presence or absence of distant metastases). It is recommended to examine at least twelve regional lymph nodes. (table 1)

- **Tumour (T)** component describes the extent to which the primary colorectal tumor has invaded the layers of the intestinal wall. Tis (carcinoma in situ) indicates that the cancer is confined to the mucosa, without invasion into the submucosa. T1 tumors invade the submucosa, while T2 tumors penetrate the muscularis propria, the muscle layer of the bowel wall. T3 tumors extend through the muscularis propria into the subserosa or pericolic/perirectal tissue, and T4 tumors invade adjacent organs or perforate the visceral peritoneum, representing locally advanced disease. Accurate determination of the T stage is essential for evaluating surgical resectability, assessing the risk of lymph node involvement, and guiding the need for neoadjuvant therapy. (Amin *et al.*, 2017)
- **Lymph node (N)** component reflects the involvement of regional lymph nodes, indicating the spread of cancer cells through lymphatic channels. N0 signifies no regional lymph node metastasis, N1 indicates metastasis in 1–3 regional lymph nodes, and N2 denotes metastasis in four or more regional lymph nodes. The presence and number of affected lymph nodes serve as strong prognostic indicators and play a crucial role in determining the need for adjuvant chemotherapy. (Amin *et al.*, 2017)

- **Metastasis (M)** component describes the presence of cancer spread beyond the regional lymph nodes. M0 indicates that no distant metastasis is detected, while M1 signifies the presence of distant metastases, most commonly affecting the liver, lungs, or peritoneum. Identifying metastasis is critical for treatment planning, guiding decisions regarding systemic chemotherapy, targeted therapy, or palliative care . (Amin *et al.*, 2017)
- By integrating the Tumor (T), Node (N), and Metastasis (M) components, colorectal cancer (CRC) can be classified into stages ranging from stage 0 (carcinoma in situ, confined to the mucosa) to stage IV, where the disease has spread to distant organs such as the liver or lungs. (Amin *et al.*, 2017)

Table 1: TNM Classification of Colorectal Adenocarcinoma (Barret *et al.*, 2009)

Pt: primary tumor	PN: Regional lymphadenopathy	PM: Distant metastases
_Tis: Intraepithelial or Basement Membrane Tumor _T1: Tumor with involvement limited to the mucosa or submucosa Inbox _T2: Tumor invading the muscularis propria Pending _T3: Tumor invading the subserosa Sent Drafts _T4: Tumor invading adjacent structures Purchases Travels Phase T4a: Peritoneal invasion of the visceral tissue Libellay T4b: Invasion of a neighboring organ	_NO: No lymph node metastasis reception _N1: 1 to 3 involved lymph nodes N1a: 1 involved lymph node N1b: 2-3 involved lymph nodes Lymph nodes sent Nic: Tumor deposits << satellite in the subserosa, or in non-peritonealized pericolic or perirectal tissue, in the absence of metastatic lymph nodes lons _N2: Involvement of 4 or more pericolic or perirectal lymph nodes or along a vascular axis Cacements N2a: 4-6 involved lymph nodes	_MO: No metastasis _M1: Presence of distant metastasis(es) M1a: Distant metastases confined to one organ Notifications on the desktop M1b: Metastases affecting more than one metastatic site or peritoneal involvement

➤ **Stage 0: Carcinoma in situ (Tis, N0, M0)**

Stage 0 represents the earliest form of colorectal cancer, also known as carcinoma in situ. At this stage, malignant cells are confined to the mucosa, the innermost lining of the colon or rectum, without invading the submucosa or muscularis propria. There is no involvement of regional lymph nodes or distant organs (N0, M0). Clinically, Stage 0 is highly curable, typically managed through local excision or polypectomy, and carries an excellent prognosis. (Edge *et al.*, 2017)

➤ **Stage I: Early Cancer (T1-T2, N0, M0)**

At this stage, the tumor invades the submucosa (T1) or the muscularis propria (T2), reflecting early local spread. There is no involvement of regional lymph nodes (N0) and no distant metastasis (M0). Clinically, Stage I tumors are considered early-stage colorectal cancer and generally have a favorable prognosis, with surgical resection alone often being sufficient for cure. (Edge *et al.*, 2017)

➤ **Stage II: Locally Advanced Cancer**

Stage II colorectal cancer is defined by local tumor extension beyond the muscularis propria. T3 tumors penetrate through the muscularis propria into the pericolic or perirectal tissues, while T4 tumors invade adjacent organs or perforate the visceral peritoneum. There is no regional lymph node involvement (N0) and no distant metastasis (M0). Stage II is further subdivided into IIA, IIB, and IIC based on the depth of tumor invasion and involvement of surrounding organs. Clinically, patients with Stage II disease may require adjuvant chemotherapy, particularly in high-risk cases, to reduce the likelihood of recurrence. (Edge *et al.*, 2017)

Stage II Subcategories (table 1)

➤ **Stage III: Regional Lymph Node Involvement**

Stage III colorectal cancer is defined by the spread of cancer cells to regional lymph nodes, while the primary tumor may remain locally confined or extend through the bowel wall. Substaging—IIIA, IIIB, and IIIC—is based on the T classification and the number of involved lymph nodes. There is no distant metastasis (M0). Clinically, lymph node involvement increases the risk of recurrence, and patients typically undergo surgical resection followed by adjuvant chemotherapy to improve outcomes. (Edge *et al.*, 2017)

➤ **Stage IV: Distant Metastasis**

Stage IV colorectal cancer indicates that the disease has spread beyond the colon or rectum to distant organs, most frequently the liver or lungs. Clinically, Stage IV represents advanced cancer that requires systemic therapy, which may include chemotherapy, targeted therapy, immunotherapy, or palliative care, depending on the patient's condition. Prognosis at this stage is generally poorer compared to earlier stages (Kraria&Lakehal, 2020).

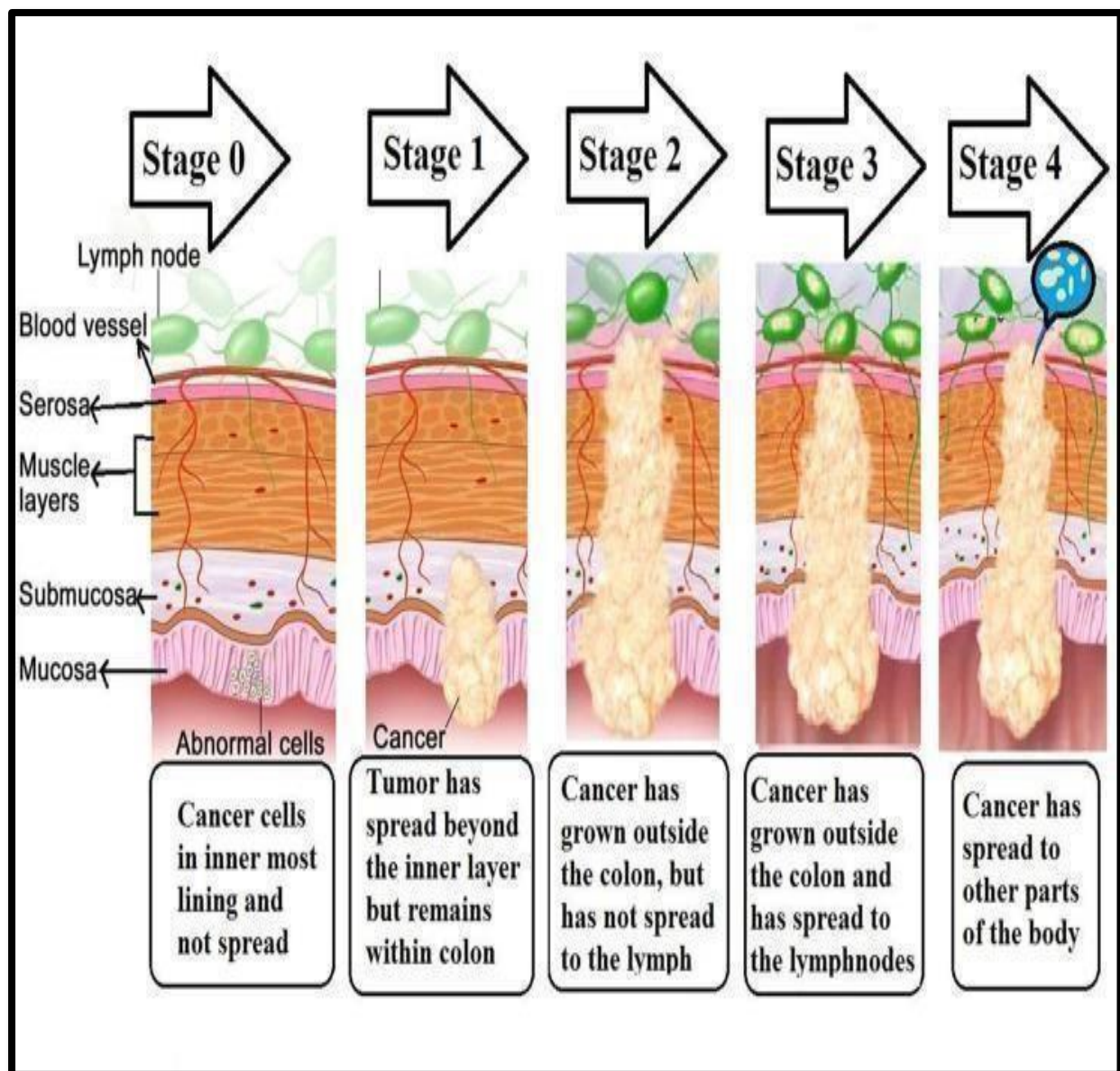


Figure 10: Stages of Colorectal Cancer Progression (Franko *et al.*,2020)

Table 2 : TNM Staging Classification of Colorectal Cancer According to the AJCC System (Barret *et al.*, 2009)

Stage 0	PTis NO MO
Stage I	PT1-2 NO MO
Stage IIA	PT3 NO MO
Stage IIB	NO pT4a
Stade IIC	PT4b NO MO
Stade IIIA	pT1-2 N1/N1c M0 or pT1 N2a
Stade IIIB	pT3-4a N1/N1c M0 or pT2-3 N2a M0 or pT1-2 N2b M0
Stade IIIC	pT4a N2a M0 or pT3-4a N2b M0 or pT4b N1-2 MO
Stage IVA	All T, all N, M1a
Stade IVB	All T, all N, M1b

10. Clinical manifestations of colorectal cancer

Colorectal cancer (CRC) is often asymptomatic in early stages. As it advances, patients may experience changes in bowel habits (diarrhea, constipation, or loose stools), rectal bleeding, persistent abdominal discomfort, unexplained weight loss, and iron-deficiency anemia. Symptoms can vary depending on whether the tumor is in the colon or rectum. (Mayo Clinic,nd.)

The manifestations of colorectal cancer may include:

- Changes in bowel habits, such as more frequent diarrhea or constipation.
- Rectal bleeding or blood in the stool.
- Persistent discomfort in the abdominal area, such as cramps, flatulence, or pain.
- A feeling that the bowels do not empty completely during a bowel movement.
- Weakness or fatigue.
- Unintentional weight loss. (Mayo Clinic, 2024)

11. Diagnostic Methods

a. Clinical examinations

Colorectal cancer screening includes colonoscopy every 10 years, flexible sigmoidoscopy every 5–10 years, and annual stool-based tests (FIT or gFOBT). Screening for average-risk adults starts at age 45 to detect cancer or polyps early.(Mayo Clinic,2024).

b. Biological examinations

Biological tests for colorectal cancer detect hidden blood or genetic markers in stool to identify polyps or cancer early. Screening usually starts at age 45 and includes FIT and gFOBT, performed annually, and stool DNA-FIT tests every three years. (National Cancer Institute, n.d.)

Main Biological and Stool-Based Tests for Colorectal Cancer Screening

- **The Fecal Immunochemical Test (FIT or iFOBT)** specifically detects human hemoglobin in the stool and does not require any dietary restrictions.
- **The Guaiac-based Fecal Occult Blood Test (gFOBT)** detects heme in the stool and requires dietary modifications, such as avoiding red meat before testing.
- **The Stool DNA-FIT (sDNA-FIT)** test detects both blood (hemoglobin) and DNA markers released by cancerous or precancerous cells in the stool.
- **The Septin 9 (Epi proColon)** test is a blood-based screening method that detects methylated DNA associated with colorectal cancer. (Gupta, 2022)

c. Endoscopic and radiological examinations

Endoscopic and radiological examinations are essential for detecting, diagnosing, and staging colorectal cancer. Colonoscopy remains the gold standard because it allows direct visualization of the entire colon, enables tissue biopsy, and permits polyp removal during the procedure. (Gupta, 2022) Radiologic imaging such as CT colonography provides detailed views of the colon and rectum and serves as a valuable adjunct, especially when colonoscopy is incomplete or contraindicated (PubMed,nd.) . These imaging methods also contribute to accurate staging and treatment planning in colorectal cancer.

➤ **Main Endoscopic Examinations**

- **Colonoscopy** is the preferred high-sensitivity test for examining the entire colon and rectum. It enables physicians to perform biopsies and remove polyps during the procedure, making it a key tool for colorectal cancer screening. . (Mayo Clinic, 2024)
- **Colon capsule endoscopy** uses a small, wireless camera capsule to capture images of the colon. Although it is non-invasive, a follow-up colonoscopy is required if any abnormalities are detected. (Smith & Doe, 2021)
- **Endoscopic Ultrasound (EUS) Used** specifically for staging rectal cancers to evaluate the depth of invasion, as explained by UT MD Anderson Cancer Center. (Liao *et al.*, 2024)

➤ **Main Radiological Examinations**

- **CT colonography**, also known as virtual colonoscopy, uses a focused CT scan of the abdomen and pelvis to create 3D images for detecting polyps and colorectal cancers. It is particularly useful for patients who are unable to undergo a conventional colonoscopy. (National Cancer Institute, 2022)
- **CT scans** of the abdomen and pelvis are primarily used for staging colorectal cancer, helping physicians determine whether the cancer has spread to other organs. (Benson *et al.*, 2022)
- **Double Contrast Barium Enema (DCBE)** is an X-ray procedure that uses barium and air to outline the colon. It is now rarely used, having been largely replaced by more advanced imaging techniques. (Benson *et al.*, 2022)

Chapter III

Prevention and Risk Reduction Strategies

1. Principles of Colorectal Cancer Treatment

The management of colorectal cancer is based on several complementary therapeutic approaches, including surgery, chemotherapy, targeted therapy, and radiotherapy. The choice of treatment depends on the stage of the disease, tumor location, and the patient's general condition (Van Cutsem *et al.*, 2016).

1.1. Surgical Treatment

Surgery represents the main treatment modality for colorectal cancer. Its primary objective is the complete removal of the primary tumor and, in some cases, metastatic lesions. The extent of surgery depends on the tumor location and the degree of local invasion (Van Cutsem *et al.*, 2016).

For early-stage lesions, local excision or polypectomy may be performed during colonoscopy when the cancer develops from a polyp. In more advanced cases, segmental resection of the affected intestinal segment is carried out, followed by restoration of intestinal continuity through anastomosis (Benson *et al.*, 2022).

The most common surgical procedures include right or left hemicolectomy, sigmoid resection, and total mesorectal excision (TME) for rectal cancer. These procedures also involve regional lymph node dissection to ensure accurate staging of the disease (Heald *et al.*, 1982).

In certain situations, particularly in low rectal tumors or intestinal obstruction, a temporary or permanent stoma (colostomy or ileostomy) may be required (Wexner & Beck, 2007).

Surgical procedures can be performed by either laparotomy (open surgery) or laparoscopy, the latter generally allowing faster postoperative recovery and reduced postoperative pain (Lacy *et al.*, 2002).

1.2. Chemotherapy

Chemotherapy aims to destroy cancer cells or inhibit their proliferation. It may be administered orally or intravenously and acts systemically throughout the body (Longley *et al.*, 2003).

The main chemotherapy regimens are based on fluoropyrimidines, particularly 5-fluorouracil (5-FU) and capecitabine. These drugs are often combined with folinic acid (leucovorin) to enhance their therapeutic effectiveness (Gramont *et al.*, 2000).

In advanced stages, chemotherapy may also be combined with other cytotoxic agents such as oxaliplatin or irinotecan, improving tumor control and patient survival (Goldberg *et al.*, 2004).

1.3. Targeted Therapy

Targeted therapy involves the use of specific agents designed to interfere with molecular pathways involved in tumor growth and progression (Van Cutsem *et al.*, 2016).

Bevacizumab is a monoclonal antibody directed against vascular endothelial growth factor (VEGF), thereby inhibiting the formation of new blood vessels necessary for tumor development (Hurwitz *et al.*, 2004).

Cetuximab and panitumumab target the epidermal growth factor receptor (EGFR), which is over expressed in certain colorectal cancer cells. Their action helps inhibit tumor cell proliferation and promote cancer cell death (Cunningham *et al.*, 2004).

1.4. Radiotherapy

Radiotherapy uses ionizing radiation to destroy cancer cells and is mainly indicated in the treatment of rectal cancer (Sauer *et al.*, 2004).

It may be administered alone or in combination with chemotherapy (chemoradiotherapy), most commonly before surgery to reduce tumor size and decrease the risk of local recurrence (Bosset *et al.*, 2006).

Surgical intervention is generally performed 6 to 8 weeks after completion of chemoradiotherapy. In selected cases, postoperative radiotherapy may also be recommended (Van Cutsem *et al.*, 2016).

Specialized techniques such as brachytherapy or contact radiotherapy may be used in certain specialized centers for the treatment of selected localized rectal cancers (Gerard *et al.*, 2003).

1.5. Immunotherapy

Immunotherapy is a modern therapeutic approach that enhances the body's immune defenses against cancer cells. It is mainly indicated for patients with colorectal cancer exhibiting high microsatellite instability (MSI-H) or deficient DNA mismatch repair (dMMR), which are associated with a better response to immune checkpoint inhibitors.

This treatment works by blocking specific proteins that inhibit immune cell activity, thereby enabling the immune system to recognize and destroy tumor cells more effectively.

The principal immunotherapeutic agents currently used in colorectal cancer management include pembrolizumab and nivolumab, particularly in advanced or metastatic forms of the disease (André *et al.*, 2020).

2. Treatment of Malignant Polyps

A malignant polyp is defined as a colorectal polyp containing invasive carcinoma. The therapeutic management of these lesions depends mainly on the depth of tumor invasion within the polyp or the intestinal wall, as well as the presence of unfavorable histopathological features identified during microscopic examination.

2.1 Malignant Polyps of the Colon

For malignant colonic polyps presenting no invasion or only low to intermediate levels of invasion, endoscopic polypectomy alone may be considered sufficient treatment. This conservative approach is appropriate when complete excision is achieved and no adverse histological characteristics are identified.

However, in cases showing deep invasion or unfavorable histopathological findings, additional surgical management is recommended. This usually consists of segmental or standard colectomy associated with regional lymph node dissection in order to reduce the risk of residual disease and lymphatic spread (Van Cutsem *et al.*, 2016).

2.2 Malignant Polyps of the Rectum

In rectal malignant polyps with absent or limited invasion, local excision using transanal endoscopic microsurgery (TEM) may provide adequate treatment while preserving anorectal function.

Conversely, when the lesion demonstrates extensive invasion or unfavorable histological features, a more radical surgical procedure known as total mesorectal excision (TME) is recommended. This intervention involves complete removal of the rectum and surrounding mesorectal lymphatic tissue to ensure optimal oncological control (Heald *et al.*, 1982).

For patients who are not suitable candidates for extensive surgery, postoperative chemo radiotherapy may be proposed as an alternative therapeutic strategy.

When invasive carcinoma is diagnosed on biopsy and local treatment through Tran is anal endoscopic microsurgery is planned, preoperative chemo radiotherapy may be administered in order to reduce tumor extension and improve local disease control.

In selected cases, specialized local treatments such as brachytherapy or contact radiotherapy can also be considered as alternatives to conventional surgery, with or without associated chemo radiotherapy.

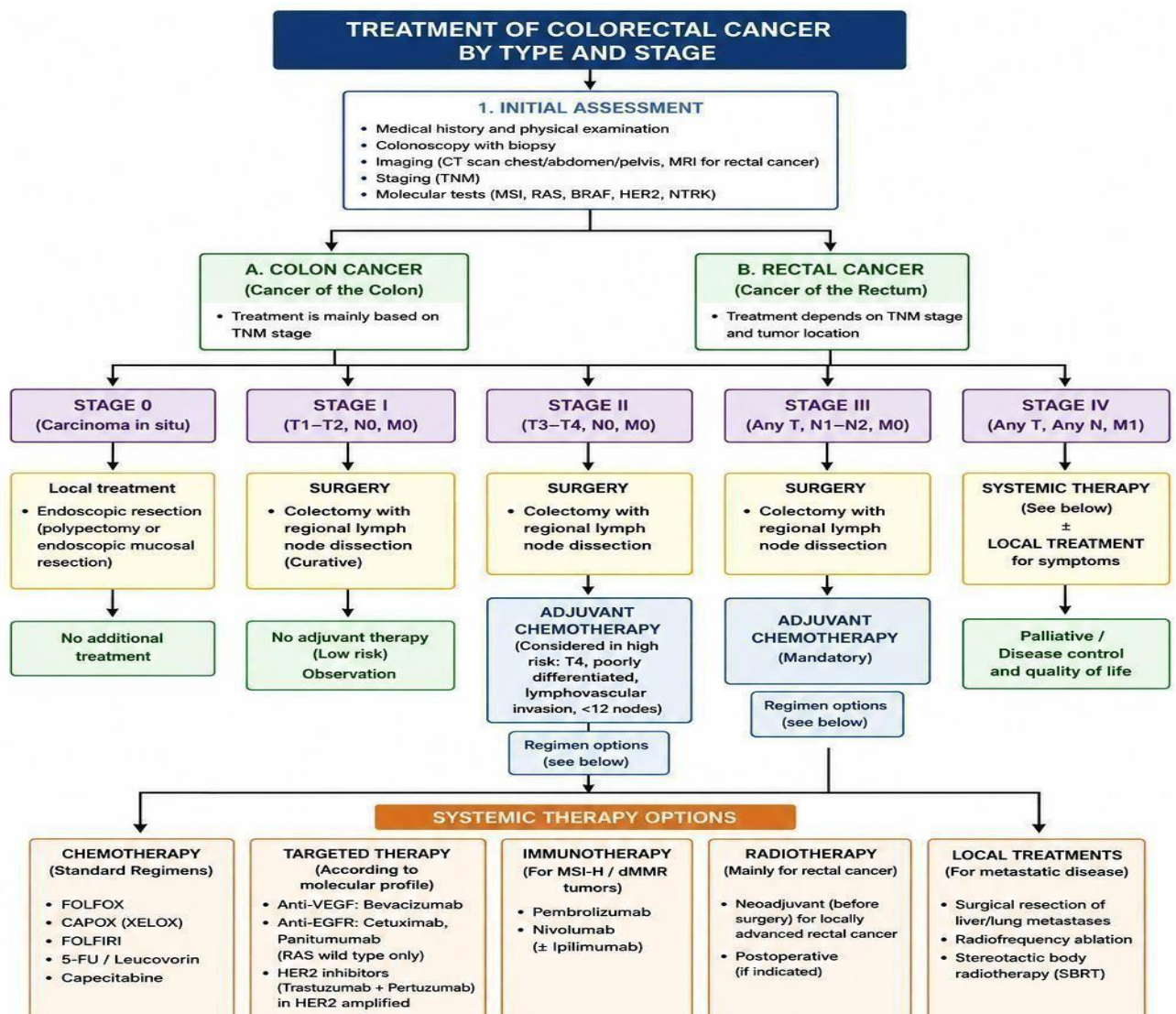


Figure 11: Flowchart of Colorectal Cancer Treatment According to Tumor Type and Stage (NCCN , 2025) and (ESMO, 2023)

3. Prevention

Prevention of colorectal cancer is based on reducing exposure to risk factors and promoting healthy lifestyle habits. Preventive strategies include maintaining a balanced diet rich in fruits, vegetables, and dietary fiber, engaging in regular physical activity, avoiding smoking and excessive alcohol consumption, and maintaining a healthy body weight. Early screening and regular medical follow-up are also essential for detecting precancerous lesions and reducing the incidence and mortality associated with colorectal cancer.

3.1. Primary prevention

Primary prevention of colorectal cancer focuses on reducing the incidence of the disease by controlling modifiable risk factors. It mainly involves lifestyle and environmental interventions, including dietary habits, physical activity, and avoidance of harmful exposures. These strategies aim to prevent the initiation of carcinogenic processes and promote overall health.

3.2. Dietary recommendations

Numerous epidemiological studies have demonstrated significant associations between dietary habits and the risk of colorectal cancer, although the levels of evidence vary. Some of these associations are considered convincing, corresponding to the highest level of evidence according to current scientific standards (Veetil *et al.*, 2021).

High consumption of red meat and excessive alcohol intake has been shown to a significant increase in the risk of colorectal cancer. These effects are largely due to the formation of carcinogenic compounds during high-temperature cooking methods, as well as to the genotoxic and pro-inflammatory effects of alcohol on the intestinal lining. Conversely, adequate intake of dietary fiber and calcium, supplemented by regular consumption of fermented dairy products such as yogurt, is associated with a reduced risk. Fiber improves bowel function and reduces the contact time between carcinogens and the colonic epithelium, while calcium plays a protective role in the intestinal mucosa, particularly by binding to certain secondary bile acids. (Schwingshackl *et al.*, 2021)

Furthermore, Evidence described as “highly suggestive” indicates that moderate alcohol consumption (between one and four drinks per day) may also to be associated with an increased risk of colorectal cancer. In addition, high consumption of dairy products appears to have a

protective effect, likely due to their high calcium and probiotic content, which may have a positive influence on the gut microbiota. (Huncharek *et al.*, 2009)

So-called “suggestive” associations also imply that a Western-style diet, rich in processed meats, saturated fats, and refined sugars, is linked to an increased risk of colorectal cancer. Similarly, adopting diets considered protective, such as the Mediterranean diet, the pescatarian or semi-vegetarian diet, as well as regular consumption of whole grains, fruits, and vegetables and adequate calcium intake, may help reduce the risk. This is largely due to their high content of fiber, antioxidants, and bioactive micronutrients. (Schwingshackl *et al.*, 2021)

Table 3: The health benefits of anti-inflammatory foods for patients with colorectal cancer (Hochenauer, 2025)

Food type	Examples	Benefits
Omega-3 fatty acids	Salmon, sardines, walnuts	Reduce intestinal inflammation and may inhibit tumor growth.
Fruits and vegetables	Berries, tomatoes, broccoli	Associated with a reduced risk of CCR, thanks to their antioxidant and fiber content.
Spices and herbs	Turmeric, ginger, garlic	Curcumin, a compound found in turmeric, has anti-inflammatory and anticancer properties.
High-fiber foods	Whole grains, legumes	Contribute to optimal gut health and a reduced risk of CRC (Colorectal Cancer)
Green	—	The polyphenols in green tea, particularly catechins, are associated with protection against CCR due to their anti-inflammatory and antioxidant properties.
Oilseeds	Almonds, chia seeds	Rich in omega-3 fatty acids and fiber, they promote good gut health

In addition, lifestyle factors play a crucial role in the process of colorectal carcinogenesis. Regular physical activity is associated with improved bowel motility and reduced systemic inflammation, whereas physical inactivity and obesity are established risk factors. Smoking has also been identified as a factor that exacerbates the progression of this disease. Nevertheless, some associations are still supported by limited evidence and require further research to validate their validity (Keum & Giovannucci, 2019).

3.3. Reduction of environmental exposure

The Mediterranean lifestyle is considered a holistic approach that goes beyond nutrition that also encompasses regular physical exercise, active transportation, and moderate-intensity daily activities. This behavioral aspect helps reduce sedentary behavior a recognized risk factor for colorectal cancer while optimizing metabolic and immune balance (Tonstad *et al.*, 2014).

Furthermore, this lifestyle emphasizes social and cultural aspects such as shared meals, seasonal eating, and a simple diet. These factors indirectly contribute to reducing exposure to environmental risks by promoting a higher quality of life and a more authentic, less processed diet (Trichopoulou *et al.*, 2014).

Consequently, the Mediterranean lifestyle serves as a comprehensive model for prevention, combining healthy nutrition, regular physical activity, and psychosocial well-being. It is an effective approach for reducing the environmental and behavioral risk factors associated with the development of colorectal cancer (Hochenauer, 2025).

4. Secondary prevention

4.1 Colorectal Cancer Screening

Colorectal cancer screening is a crucial public health strategy based on the early identification of precancerous lesions and cancers in their asymptomatic stages. According to the World Health Organization (WHO), screening refers to the use of to identify individuals who appear healthy but may have a disease, without necessarily establishing a definitive diagnosis. Individuals with positive or inconclusive results should then be referred for further diagnostic testing. (WHO, 2020)

Colorectal cancer is a disease particularly well-suited to screening due to its high prevalence, the presence of early, slow-growing, and identifiable lesions, and the availability of reliable and

effective tests. Screening helps reduce the incidence and mortality rate of the disease, primarily through the detection and removal of adenomatous lesions, while also reducing the need for complex surgical procedures. (Lieberman *et al*, 2009)

Scientific data from research consistently show that screening programs lead to a significant reduction in colorectal cancer mortality, with benefits that outweigh any potential risks. However, its effectiveness depends on several key factors, including the accuracy of the test used, the level of engagement among the target population, the frequency of screening exams, and the quality of treatment for abnormalities identified at an early stage.

Implementing a screening program remains a complex task that requires strict organization. It relies on patient engagement particularly through fecal occult blood tests and preparation for colonoscopy as well as on the availability of qualified healthcare professionals to perform endoscopic examinations and pathological evaluations. (WHO, 2023; Lieberman *et al*, 2009; ESMO, 2020)

Furthermore, the successful implementation of such programs is closely linked to the healthcare system's ability to provide high-quality services in sufficient quantities and at the appropriate times. It also depends on financial and human resources, particularly in the fields of gastrointestinal endoscopy and pathology.

From an organizational standpoint, the implementation of a screening program initially leads to an increase in the number of identified cases, due to the detection of prevalent cases, which can place additional strain on healthcare facilities. However, in the long term, early detection helps reduce advanced forms of the disease and decreases the need for intensive cancer treatments. (WHO, 2023; Lieberman *et al*, 2009; ESMO, 2020)

It therefore seems essential to implement screening program gradually to ensure its availability and prevent the overburdening of healthcare services. It is essential to conduct a thorough assessment to determine the target population, calculate the required resources, and ensure that the expected benefits outweigh the risks and organizational constraints.

Finally, the effectiveness of a screening program must be evaluated based on various criteria, including the performance of the test used, the quality of diagnosis and treatment, and the economic and organizational implications. Regular and ongoing evaluation ensures that the program meets the required standards while promoting its continuous improvement. (Smail *et al.*, 2020)

4.2 Early detection of precancerous lesions

- The early detection of precancerous lesions, such as adenomatous polyps, before they become cancerous is at the heart of colorectal cancer screening. This approach not only facilitates early diagnosis of the disease but also helps prevent it through prompt intervention. (American Cancer Society, 2023)
- The primary tool for this screening is an immunological test designed to detect the presence of occult blood in the stool. Simple to perform, non-invasive, and capable of being done at home, this test can detect microscopic bleeding that may indicate the presence of polyps or early-stage tumors. With an estimated sensitivity of between 70% and 80%, this test is effective for early detection. (WHO, 2023)
- However, some precancerous lesions do not cause consistent bleeding, which can lead to false-negative results. For this reason, it is recommended that individuals at average risk generally, those aged 50 to 74 undergo this test every two years. (WHO, 2023)
- If the test is positive, a colonoscopy is always recommended. This procedure provides a direct view of the colon lining and allows for the immediate identification and removal of polyps, thereby preventing their progression to invasive cancer. (Lieberman *et al*, 2009)
- The early identification of at-risk individuals also relies on an analysis of personal and family medical history, in addition to the possible observation of telltale gastrointestinal symptoms (rectal bleeding, bowel dysfunction, anemia of unknown origin).

For individuals classified as high or very high risk, specific follow-up via colonoscopy is recommended, sometimes in conjunction with genetic monitoring (ESMO, 2020).

- Organized screening therefore plays a crucial role in reducing the incidence and mortality of colorectal cancer, as it facilitates the identification and treatment of precancerous lesions before they progress to more advanced stages (Institut National du Cancer, 2022).

5. Health Awareness and Education

Health education and awareness are key factors in the prevention of colorectal cancer. The goal is to educate the public about risk factors, promote healthy habits, and encourage participation in screening tests, thereby helping to reduce the incidence and mortality rates associated with this disease (Hochenauer, 2025).

5.1 Objectives of the health awareness campaign

Health awareness campaigns play an important role in colorectal cancer prevention by educating the public about risk factors and promoting healthy lifestyle habits. These campaigns encourage balanced nutrition, regular physical activity, smoking cessation, and reduced alcohol consumption in order to decrease colorectal cancer risk (Jemal *et al.*, 2023).

They also aim to increase participation in screening programs and improve early detection of precancerous lesions and colorectal cancer. Furthermore, public education helps reduce misinformation and promotes better awareness of preventive healthcare practices.

5.2. To raise awareness of risk factors:

Public health initiatives highlight the major risk factors for colorectal cancer, including an unbalanced diet, a sedentary lifestyle, smoking, alcohol abuse, and obesity. The goal is to make this information accessible to promote a better understanding among the public of the risks associated with lifestyle choices. (Jemal *et al.*, 2023)

5.3. Encouraging preventive behaviors:

Health education promotes the adoption of a balanced lifestyle, which includes a high-fiber diet (fruits, vegetables, whole grains), regular physical activity, and maintaining a healthy body weight. It is crucial to convey this advice in a clear and engaging manner to encourage lasting behavioral change.

5.4. Promoting early screening:

Even though screening is considered a form of secondary prevention, promoting its importance can strengthen public commitment to screening programs, thereby facilitating the early identification of precancerous lesions.

5.5. Communication strategies in the health sector

- National health programs: National initiatives play a crucial role in spreading prevention messages, such as the National Nutrition and Health Program (PNNS), which aims to promote balanced nutrition and physical activity. Its key messages include “Eat Well, Stay Active,” “Eat 5 fruits and vegetables a day,” and “For your health, avoid consuming too much fat, sugar, or salt: Actions such as Mars Bleu aim to raise public awareness of colorectal cancer through media campaigns, seminars, and local outreach efforts.

5.6. Future Perspectives

The integration of digital technologies and social media into public health communication strategies is essential for expanding the reach of health messages, particularly among younger audiences, given the evolving nature of these strategies. Furthermore, healthcare professionals play a crucial role in raising public awareness and encouraging people to participate in screening programs (Eysenbach, 2011).

It is essential to regularly evaluate the effectiveness of public awareness campaigns in order to tailor messages to the actual needs of the population. Furthermore, strengthening cooperation among healthcare facilities, government authorities, and private stakeholders would promote a more efficient use of resources and lead to significant improvements in public health outcomes (Labonté *et al.*, 2018).

6. Future Research Directions

Building on this work, various avenues of research could be explored to enhance our overall understanding of colorectal cancer, particularly with regard to psychological and behavioral aspects:

- It is recommended, first and foremost, to conduct a more in-depth study of the role of psychological factors such as body image, anxiety, and depression in patients with colorectal cancer. Findings suggest that these variables may be influenced by how patients perceive their illness and the associated treatments, particularly in specific contexts such as the presence of a temporary stoma. Consequently, analyzing patients' cognitive and emotional representations could provide a better understanding of adaptation processes and help identify factors that influence psychological distress. The development and validation of assessment tools tailored to these specific clinical contexts also represent a major objective. (Farquharson *et al.*, 2019)
- Second, the study of the social sharing of emotions represents a promising area of research. Patients' ability to articulate their feelings and share their experiences of illness is crucial for emotional regulation and psychological adjustment. Conversely, suppressing this emotional expression could be linked to increased anxiety, depression, and, possibly, a deterioration in overall health. It would therefore be worthwhile to examine the factors that influence this emotional sharing, particularly feelings of shame or guilt, which are especially pronounced in some patients.

- Furthermore, incorporating sociocognitive methods into colorectal cancer research could lead to a better understanding of the interactions between psychological, behavioral, and biological factors. These methods would help refine management strategies by taking into account not only medical factors but also the patient's psychosocial aspects (Manne *et al.*, 2015).
- The development of new approaches to prevention and support, including specific educational and psychological interventions, is an essential step forward. The use of digital technology and innovative tools could also improve patient follow-up and encourage their participation in prevention and screening programs.
- These various research approaches pave the way for a more comprehensive and personalized approach to colorectal cancer care, one that is patient-centered and tailored to each patient's specific needs (Faury, 2018).

Practical Part

1. Study Objectives

A. Primary Objective

The primary objective of this study was to identify and evaluate risk factors associated with colon cancer by comparing patients with this disease to a disease-free control group, in order to determine the most frequent and statistically significant factors.

B. Secondary Objectives

This study also aimed to:

- ❖ Describe the sociodemographic characteristics of patients with colon cancer;
- ❖ Investigate the influence of dietary habits on the occurrence of colorectal cancer;
- ❖ Evaluate the impact of lifestyle factors (smoking, physical activity, alcohol consumption, etc.);
- ❖ Investigate the role of personal and family medical history in the development of colon cancer;
- ❖ Compare the frequencies of risk factors between the patient group and the control group;
- ❖ Determine the factors most strongly associated with colorectal cancer based on the statistical results obtained using IBM SPSS Statistics.

2. Study Type, Location, and Period

This was an analytical, observational, epidemiological case-control study. It was conducted in the oncology department of the Ahmed Francis Hospital in Oued Rhiau (Relizane, Algeria). Data collection lasted for a three-month period, from February to May 2026.

3. Study Population

We included a total of 202 participants, divided into two distinct groups:

- **The Case Group (n=162):** Consisting of 162 patients with colon cancer confirmed by histopathological examination, who were followed up or hospitalized in the oncology department during the study period.
- **The Control Group (n=40):** Consisting of 40 individuals without colon cancer, selected during the same period to serve as a comparison group.

4. Inclusion and Exclusion Criteria:

- **Inclusion Criteria:** All participants (cases and controls) who agreed to participate and were able to complete the questionnaire. Cases had to have a histologically confirmed diagnosis of colon cancer, while controls had to have no known history of colorectal cancer.
- **Exclusion Criteria:** Patients with other exclusive types of gastrointestinal cancers (such as isolated rectal cancer, small intestine cancer, or stomach cancer), individuals with cognitive or communication difficulties preventing a proper interview, or those with incomplete questionnaires.

5. Data Collection

Data were collected using a standardized, anonymous questionnaire administered directly to the participants through face-to-face interviews. The questionnaire explored the following parameters:

- **Sociodemographic data:** Age, sex, marital status, occupation, education level, and place of residence.
- **Dietary habits:** Consumption of red meat, dietary fiber, fruits and vegetables, and the frequency of fast food or processed meat consumption.
- **Lifestyle:** Smoking status (and quantity in pack-years), and physical activity level.
- **Medical and family history:** First-degree family history of colorectal cancer, personal history of intestinal polyps, or inflammatory bowel disease (IBD).
- **Clinical data (Cases only):** Duration of illness, cancer stage at diagnosis (TNM classification), and treatment protocols followed.

6. Statistical Analysis

The collected data were coded, entered, and analyzed using IBM SPSS Statistics version 27.0. The statistical analysis was conducted in two main phases:

❖ Descriptive Analysis:

- **Qualitative variables** were expressed as frequencies and percentages (%).
- **Quantitative variables** were expressed as means $\pm$ standard deviations (or as medians, depending on the normality of the distribution).

- **Comparative (Bivariate) Analysis:** * Proportions between the case group and the control group were compared using Pearson's chi-squared test (χ^2) (or Fisher's exact test when the expected frequencies in cells were less than 5). Means for quantitative variables were compared using Student's t-test for independent samples.
- **Measure of Association:** The strength of the association between exposure to the various risk factors and the occurrence of colon cancer was estimated by calculating **Odds Ratios (ORs)** and their **95% confidence intervals (95% CIs)**.
- For all statistical tests, the significance threshold was rigorously set at **p<0.05**.
- The results are presented in the form of tables and graphs.

Results

i. Descriptive study:

A. Sociodemographic variables

1. Sex

In our study involving 162 colorectal cancer cases, an analysis of the distribution of patients by sex indicates a slight predominance of women in our study sample. Indeed, women accounted for 51% of the identified cases (83 patients), while men accounted for 49% (79 patients), corresponding to a sex ratio of 1.04 women for every man.

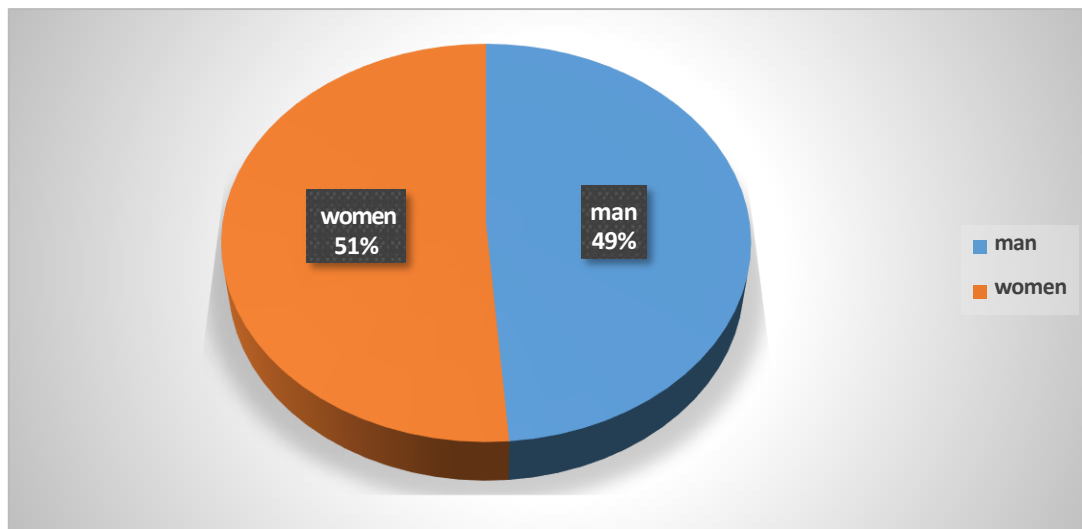


Figure 12: Breakdown by gender

2. Age

The distribution of patients with colorectal cancer according to age shows a clear predominance of the age group of 60 years and older, which accounts for 53.8% of cases ($n = 86$), making it the most affected age category.

It is followed by the 50–59 years age group with 18.1% ($n = 29$), then by patients under 40 years of age with 16.9% ($n = 27$). The 40–49 years age group is the least represented, accounting for 11.3% ($n = 18$).

This distribution confirms that colorectal cancer primarily affects older individuals, with a marked increase in frequency after the age of 60. It therefore highlights age as a major risk factor for the onset of this disease, with incidence increasing progressively with age.

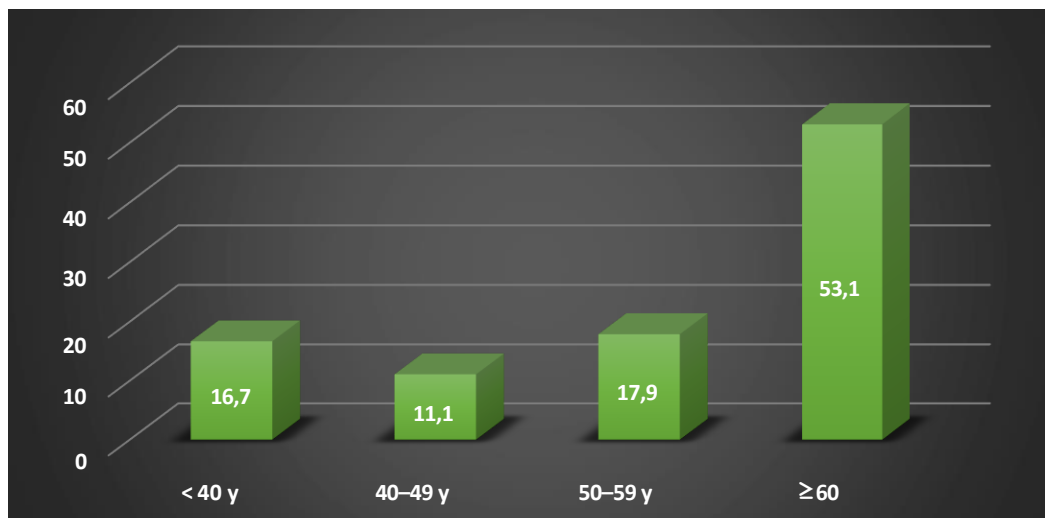


Figure 13: Distribution of patients with colorectal cancer by age

3. Employment Status of Patients

The graph shows that most patients diagnosed with colorectal cancer are unemployed, accounting for approximately 55% of the total. A significant proportion—nearly 50%—are retirees. However, it should be noted that employed patients represent the lowest percentage, at approximately 35%.

These results can be attributed to the higher incidence of colorectal cancer among older adults, who are generally retired, as well as among individuals living in precarious socioeconomic conditions. The association of unemployment and retirement may exacerbate the risk of developing this disease with reduced physical activity and less healthy lifestyles.

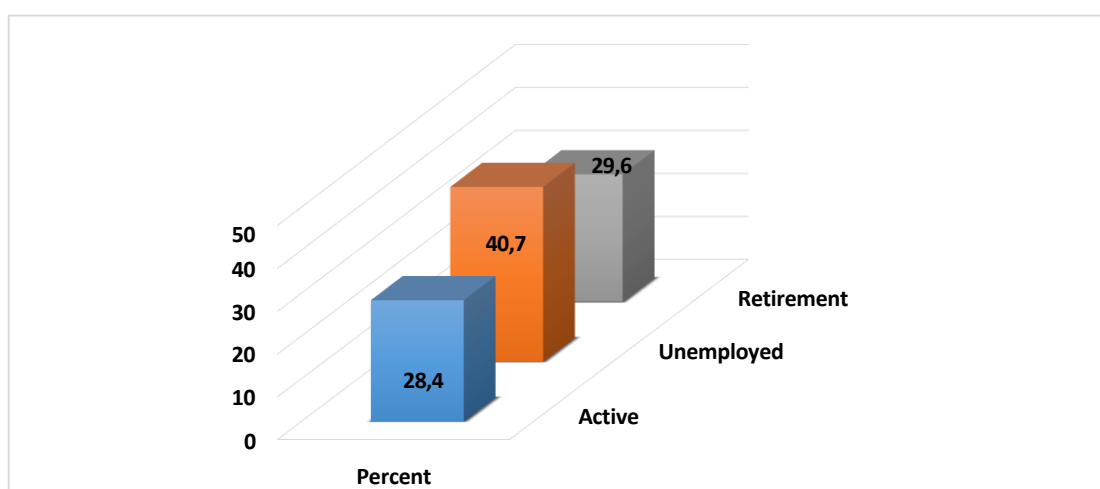


Figure 14: Distribution of patients diagnosed with colorectal cancer by occupation.

4. The patient's place of residence

The analysis of the geographical distribution of patients revealed a marked concentration of cases in the municipality of Oued Rhiau, which accounted for 43.2% of the study population. The municipalities of Jdiouia (16.7%) and Ammi Moussa (14.2%) also represented a substantial proportion of the recorded cases. The remaining patients were more heterogeneously distributed across several other areas, including Hmadna (4.9%), Ain Tarek (4.3%), Ouarizan (4.3%), Ouled Sidi Mihoube (3.1%), as well as Lahlef and Ramka (2.5% each). Mazouna (1.9%) and Ouled Aiche (1.2%) showed the lowest proportions of cases.

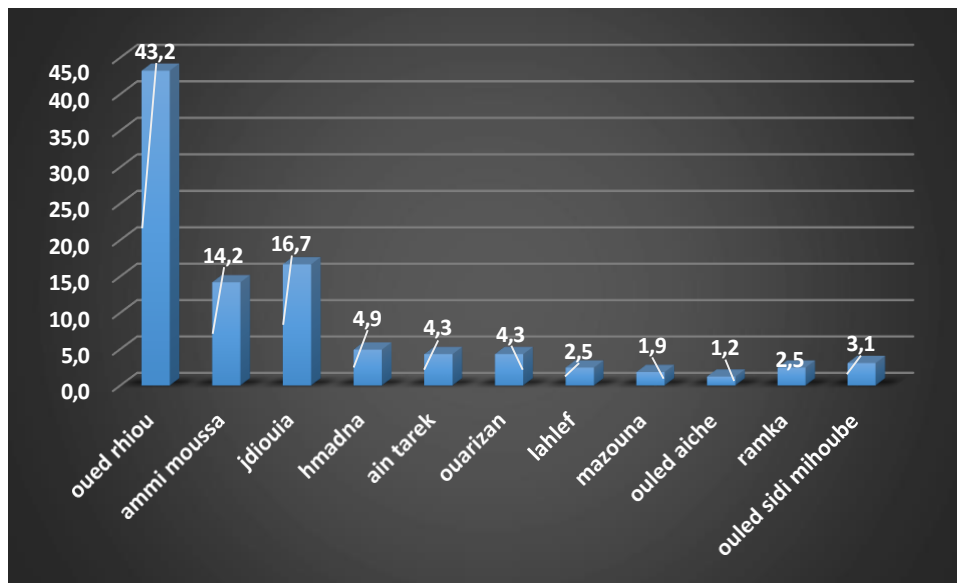


Figure 15: Distribution of patients according to their municipality of residence

B. Clinical parameters:

5. Chronic Inflammatory Bowel Diseases: Ulcerative Colitis and Crohn's Disease in Patients

The distribution of patients with colorectal cancer according to the presence of Inflammatory Bowel Diseases (IBD), such as Crohn's disease and Ulcerative Colitis, shows that a considerable proportion of patients had a history of IBD.

The data revealed that 46% of the patients, corresponding to 74 cases out of a total of 162 patients, had a previous history of IBD. In contrast, 54% of the patients, representing 86 cases, had no prior chronic inflammatory bowel disease.

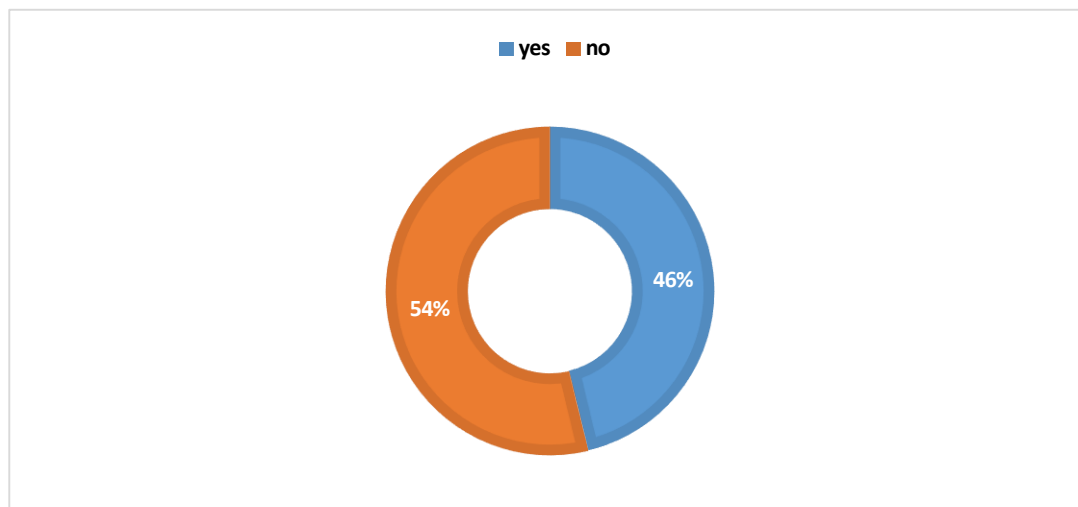


Figure 16: Distribution of patients based on a history of inflammatory bowel disease (IBD).

6. Personal History of polyps Colorectal Tumors in Patients

Distribution of patients based on their personal history of colorectal polyps.

According to the data collected, a large proportion of patients (64%) already had a personal history of colorectal polyps before being diagnosed with cancer. Conversely, 36% of patients reported no such history.

This prevalence (64%) supports the classic “adenoma-carcinoma” sequence, according to which the development of colorectal cancer is frequently preceded by the appearance of adenomatous polyps.

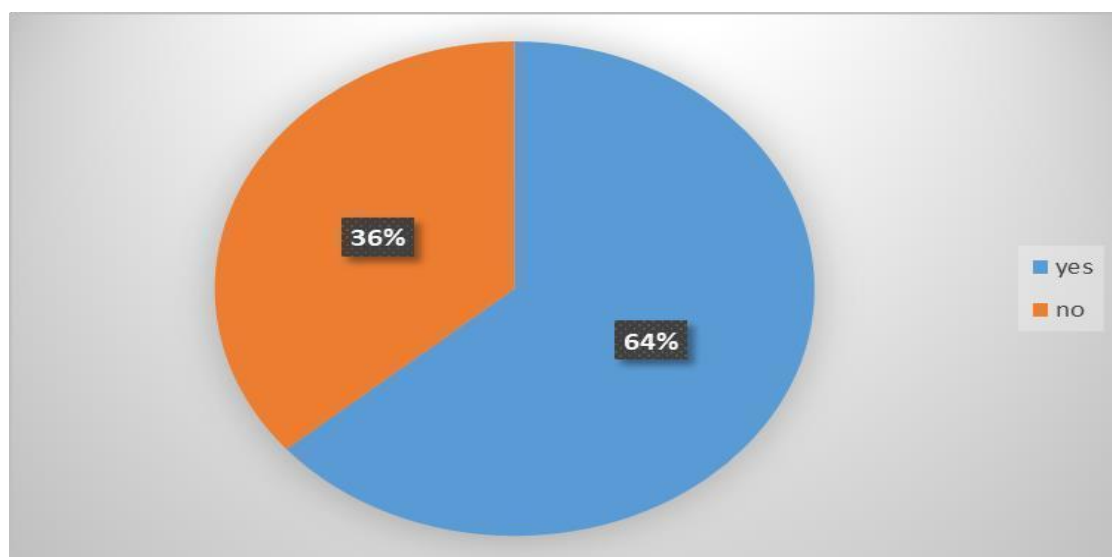


Figure 17: Prevalence of a personal history of polyps among individuals with colorectal cancer

C. Nutrition:

7. Frequency of red meat consumption

The frequency with which our sample consumes red meat.

The study reveals that an overwhelming proportion of participating patients frequently consume red meat. Specifically, nearly 78% of individuals consume it once or twice a week, while a significant 22% consume it three or more times a week. In this sample, it is virtually impossible to find patients who follow a diet that excludes red meat.

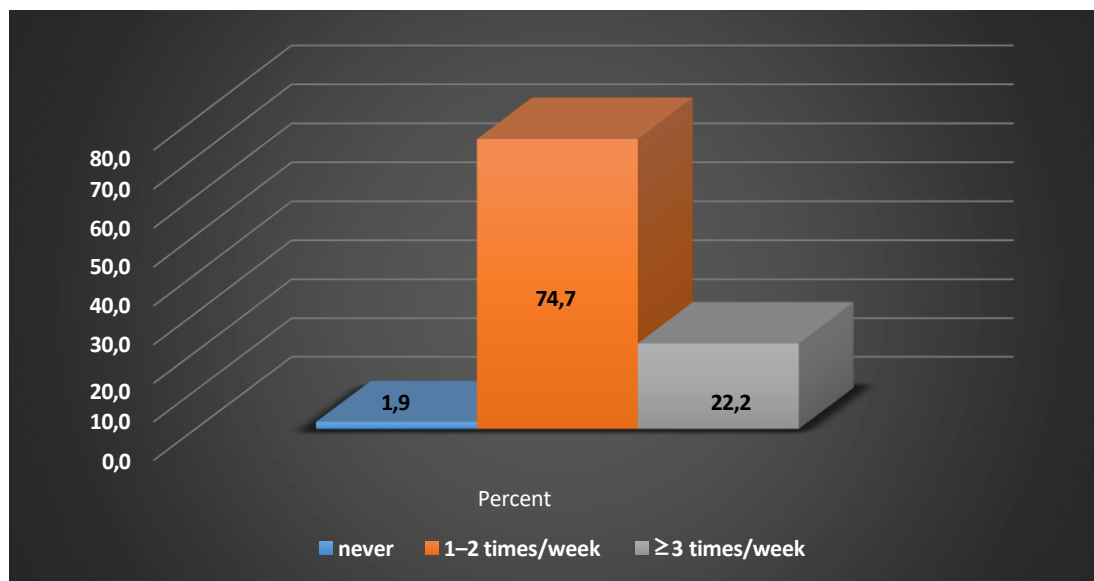


Figure 18: Breakdown of patients by their red meat consumption habits.

8. Consumption of processed meats (deli meats, nuggets, sausages)

Analysis of processed meat consumption (cured meats, dried and smoked meats) among our sample of 162 patients reveals a deeply ingrained dietary habit. Indeed, 92.6% of the study population (150 patients) include these products in their diet. More specifically, consumption patterns are predominantly moderate: 71.6% of subjects ($n = 116$) report consuming them occasionally, while 21.0% ($n = 34$) consume them regularly. Conversely, only 6.2% of patients ($n = 10$) report completely excluding processed meats from their diet.

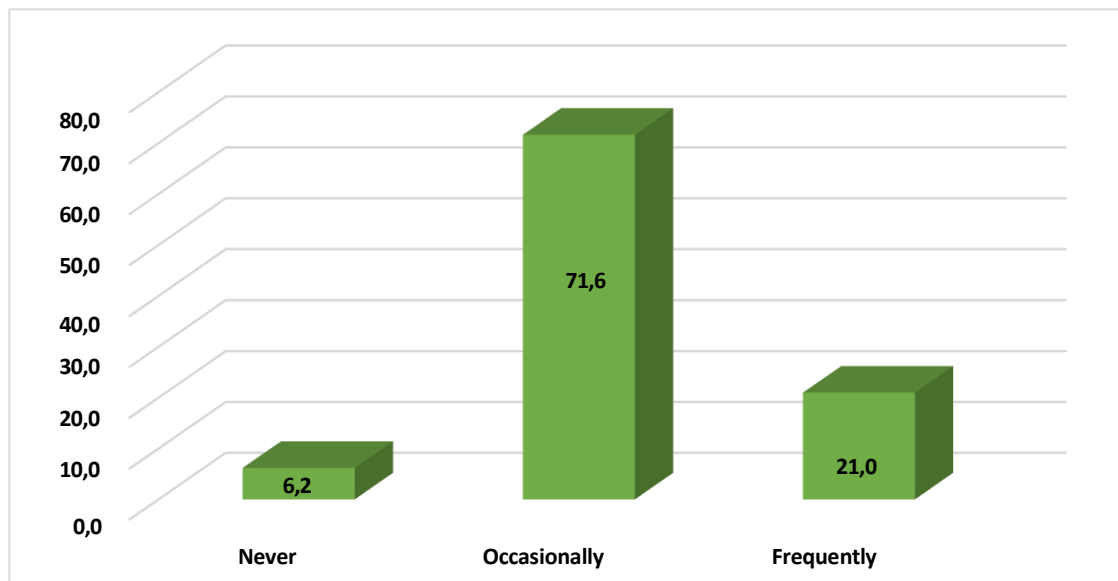


Figure 19: Frequency of consumption of processed meats among patients.

9. Consumption of frozen meats in patient

The frequency with which our patients consume frozen meat in our study.

The data show that a large proportion of patients include frozen meat in their diet to varying degrees. “Occasional” consumption is the most common, accounting for 50%, followed by “rare” (25%) and “frequent” (15%). A small proportion of patients (less than 10%) report that they never consume frozen meat.

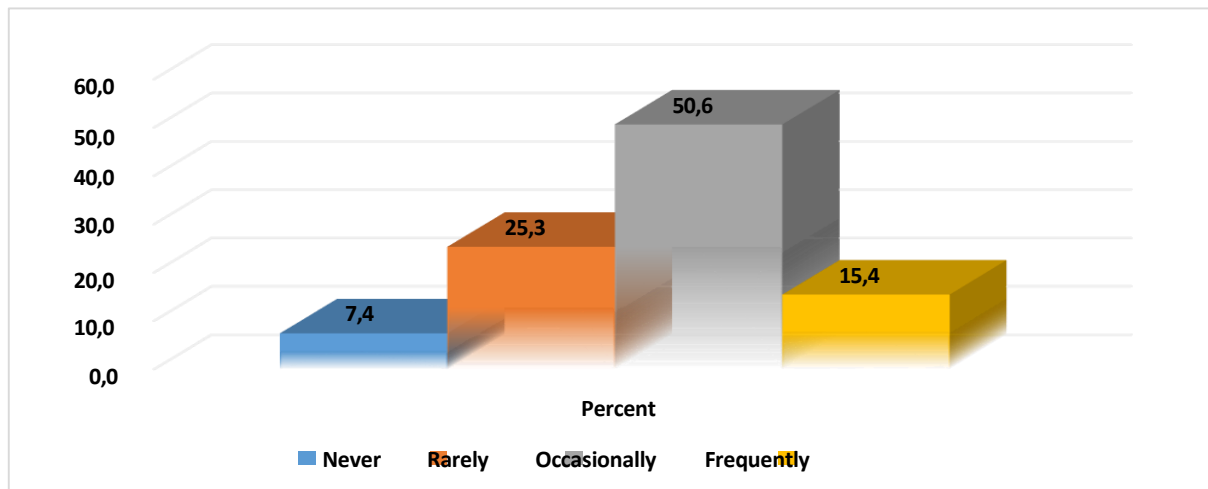


Figure 20: repetition consumption of frozen meats in-patient

10. The patient's usual method of cooking meat

The results highlight a prevalence of high-temperature cooking methods. Indeed, barbecuing and grilling rank first at 31.5%, while frying follows closely behind at 30.9%. Gentler cooking techniques, such as baking (21%) or steaming/boiling (11.7%), are considerably less common.

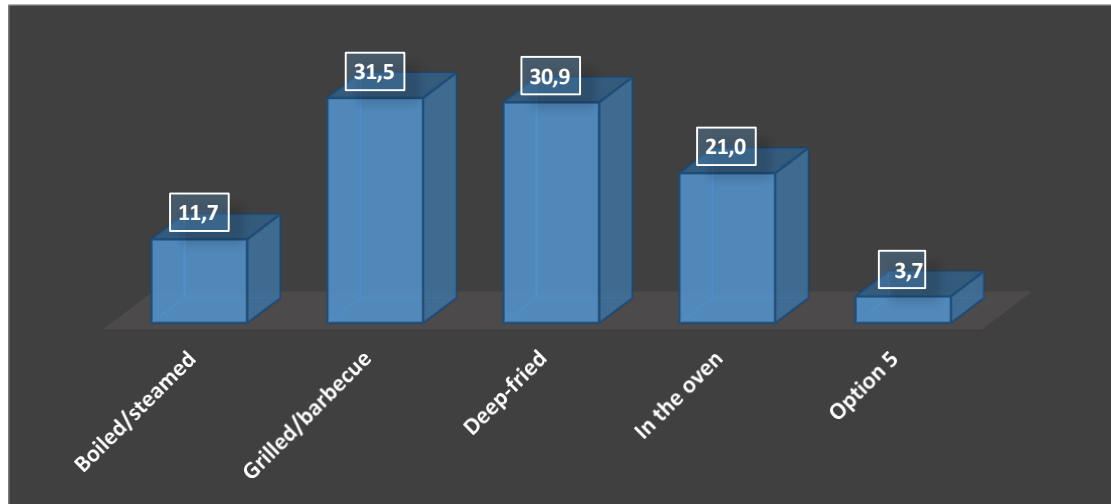


Figure 21: Breakdown of patients by their usual methods of cooking meat

11. Consumption of fresh fruit among patients

Out of 162 patients, a large proportion reported regular consumption of fresh fruits. Approximately 54% of the patients, corresponding to nearly 87 cases, reported daily fruit consumption, while 44%, or about 71 cases, consumed fruits two to three times per week. Only a small proportion of patients reported rare fruit consumption..

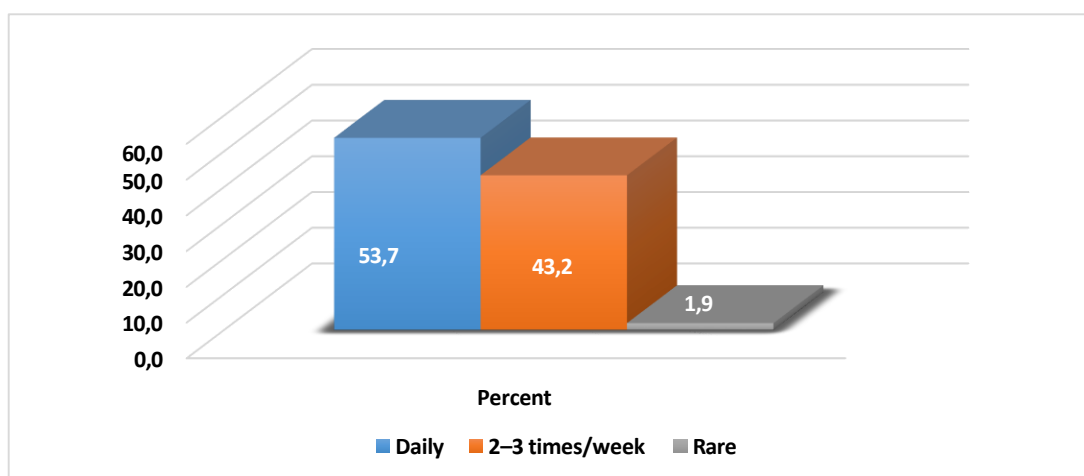


Figure 22: Breakdown of patients by their daily fresh fruit consumption habits.

12. Consumption of green vegetables among patients

The results of our study indicate generally healthy eating habits, characterized by high consumption of green vegetables among the study population. In fact, nearly 86% of patients reported eating green vegetables daily, while only a small proportion reported eating them occasionally or rarely. These findings suggest that green vegetables are a regular part of the patients' diets.

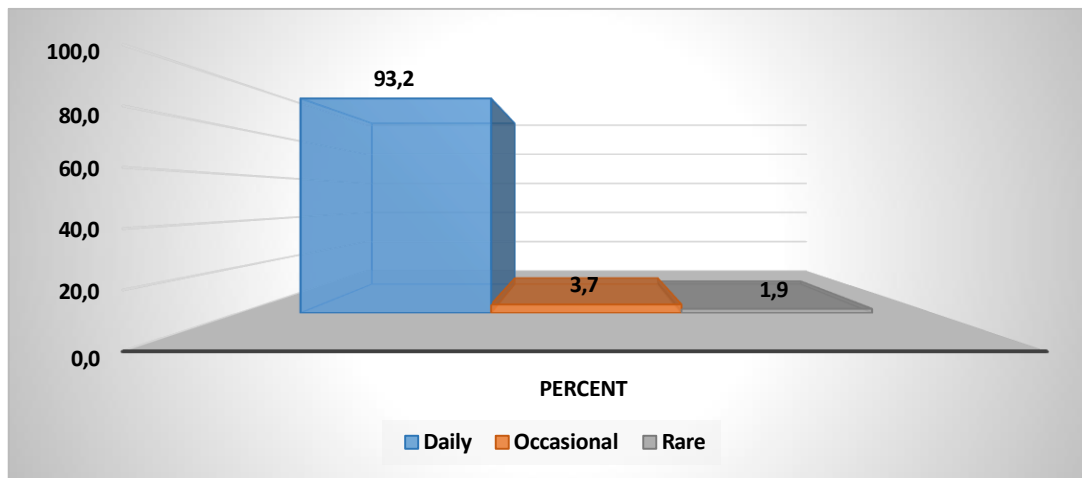


Figure 23: Frequency of green vegetable consumption among patients with colorectal cancer.

13. Consumption of fermented dairy products by patients

Our study demonstrates a high level of fermented dairy product consumption within the studied population, with 89% of patients reporting regular intake, indicating that this dietary habit is widely prevalent. Conversely, only 11% of participants reported little or no consumption, reflecting a small minority with limited or absent intake of fermented dairy products.

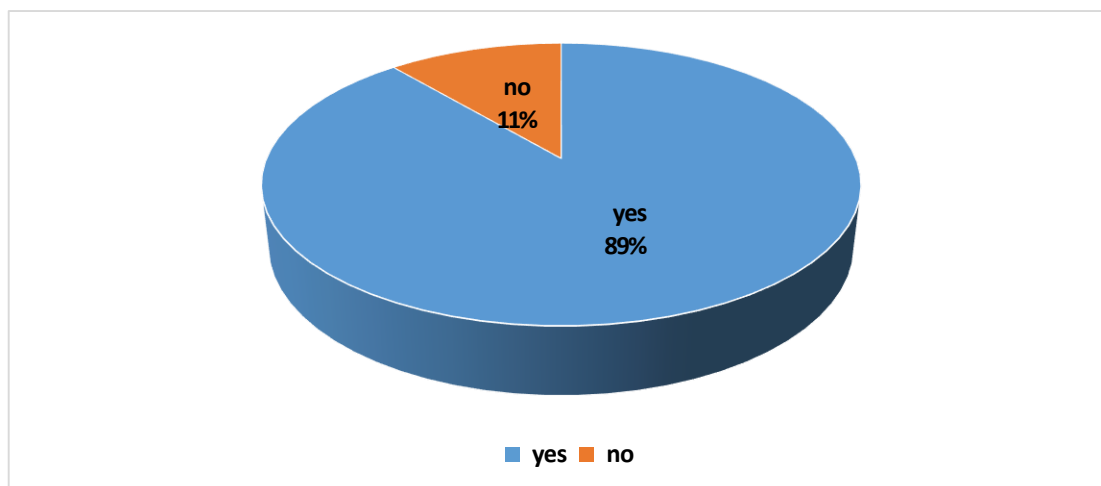


Figure 24: Frequency of consumption of fermented dairy products

14. Consumption of tea, coffee, or herbal beverages among patients

The results indicate that consumption is nearly universal and occurs on a daily basis. In fact, 96% of the patients in our sample reported drinking these beverages daily. Only a very small percentage consume them occasionally (4%) or not at all (1%).

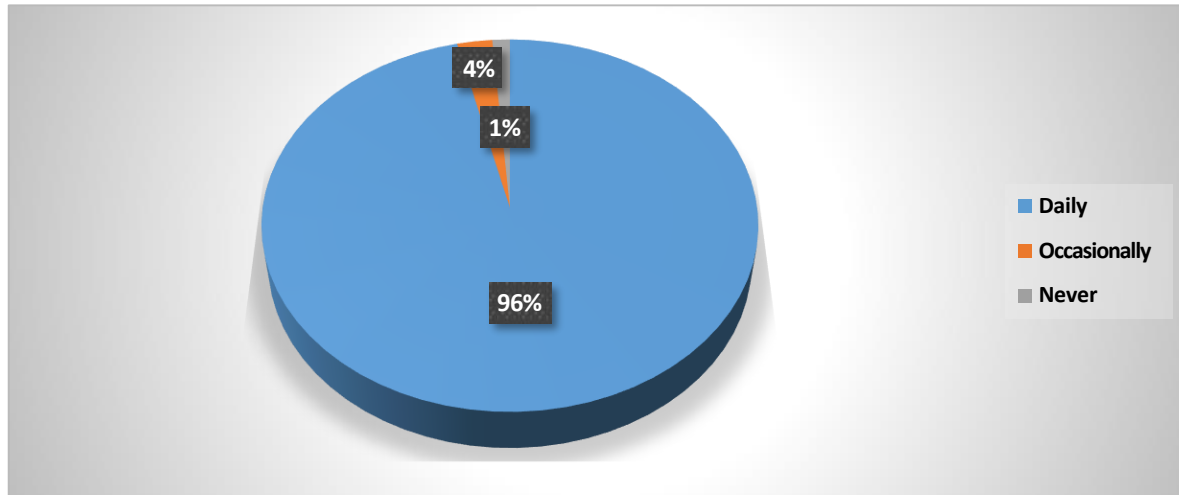


Figure 25: Frequency of consumption of hot beverages (tea, coffee, herbal teas)

D. Clinical parameters:

15. Chronic stress

According to the 162 cases included in our study, the results show a high prevalence of stress among patients. Indeed, 61.1% of participants reported high stress levels, while 32.1% reported moderate stress. Overall, more than 93% of the studied individuals experience significant stress. In contrast, only a very small proportion (1.2%) reported being completely free of stress.

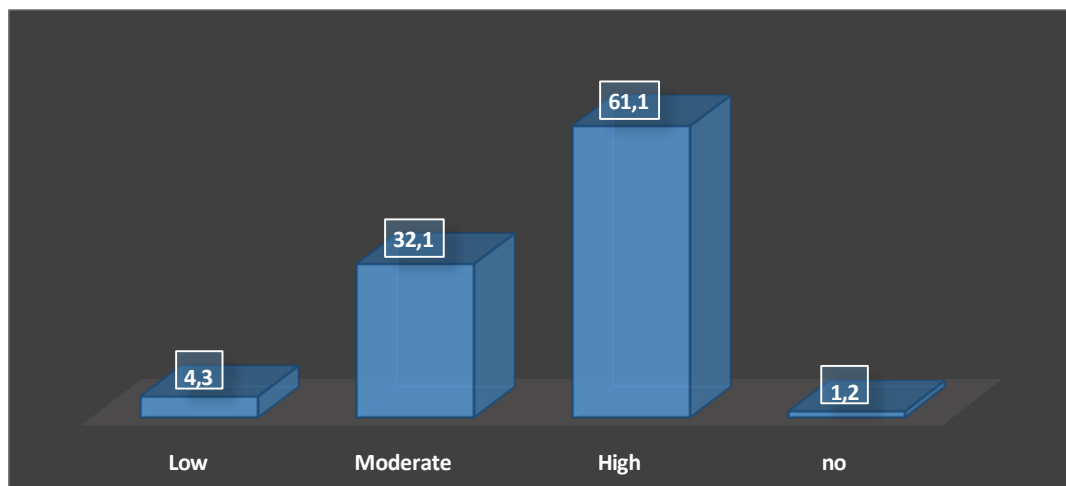


Figure 26: Distribution of patients diagnosed with colorectal cancer by level of chronic stress.

16. Symptoms present before diagnosis

The results of our study show that colorectal cancer is most often revealed by clinical symptoms before diagnosis. Bowel movement disorders are the most frequent manifestation, particularly chronic constipation, observed in 29.6% of patients.

Other symptoms were also reported, such as fatigue (16.7%), abdominal pain (16.0%), and persistent diarrhea (13.6%). More specific, but less frequent, signs include weight loss (9.3%), bloating (7.4%), and blood in the stool (6.2%). Thus, in our study population, colorectal cancer appears primarily symptomatic at the time of consultation.

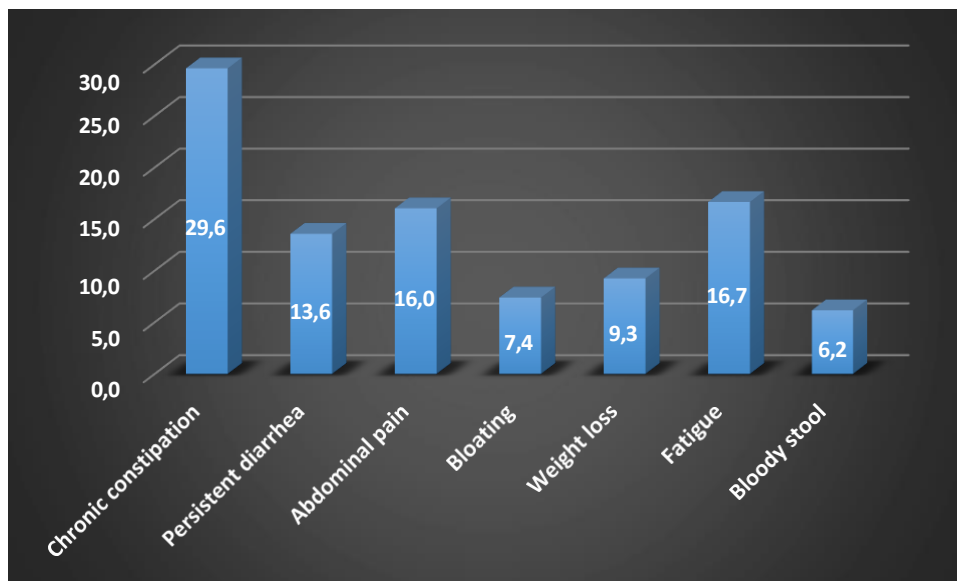


Figure 27: Distribution of clinical symptoms prior to a diagnosis of colorectal cancer.

17. Duration of symptoms before consultation

According to our study of colorectal cancer patients, the time between the onset of the first symptoms and the first medical consultation varies considerably. Indeed, 29.6% of patients consult quickly, within 3 months. However, a significant proportion delay consultation, with 38.9% of patients consulting between 3 and 6 months, and 30.2% after more than 6 months of symptom progression. Thus, nearly 70% of patients exceed the 3-month timeframe before consulting, suggesting a significant diagnostic delay.

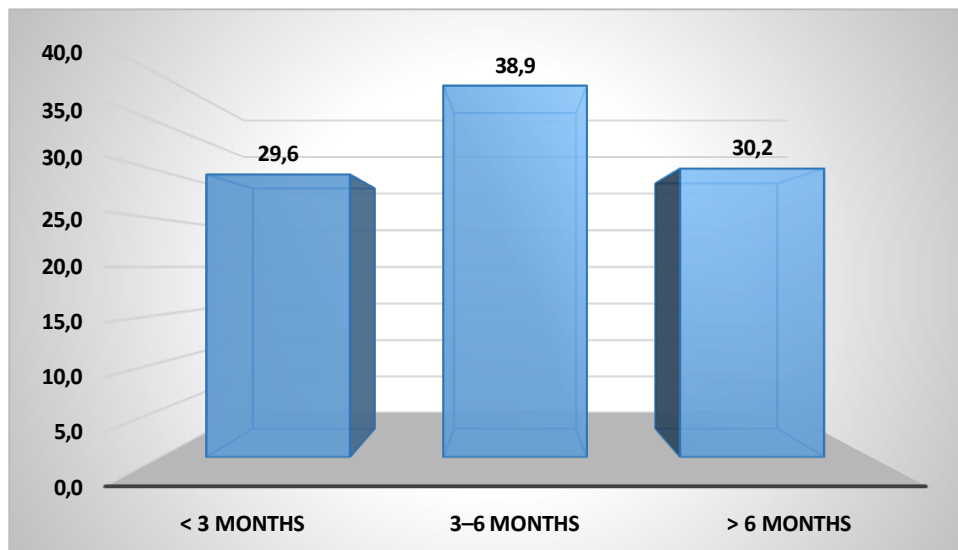


Figure 28: The time interval between the onset of initial symptoms and the patient's medical consultation.

18. History of Anemia

The results show that 19% of colorectal cancer patients have a history of anemia, while 81% do not have anemia.

These findings indicate that the majority of the studied patients do not suffer from anemia. However, the presence of anemia in some patients may be associated with chronic bleeding caused by the colorectal tumor. Therefore, anemia remains an important clinical sign that may contribute to the diagnosis and follow-up of colorectal cancer patients.

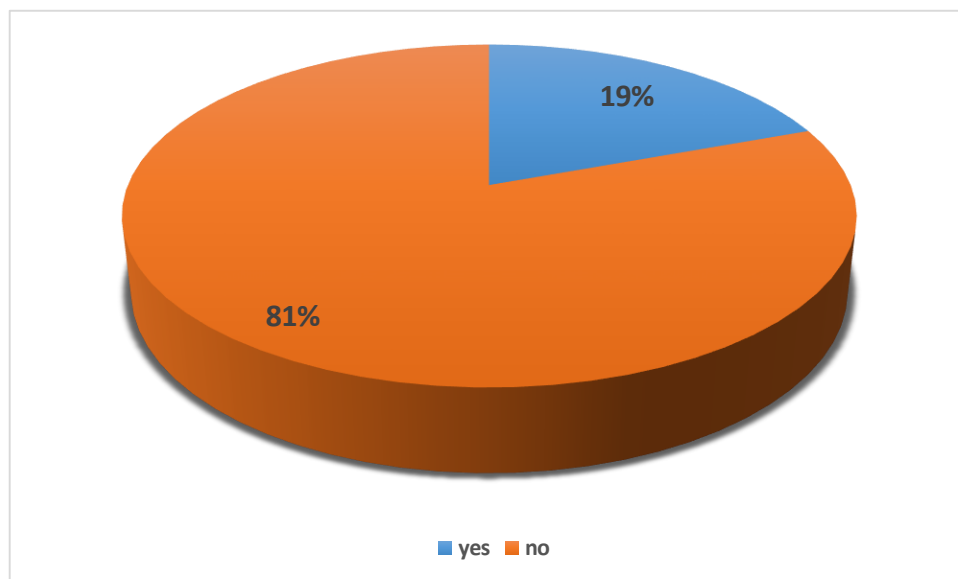


Figure 29: Prevalence of a history of anemia

19. Screening for previous colorectal cancer

In the studied population, the results show a low rate of colorectal cancer screening. Indeed, 61% of participants had never undergone screening before, while only 39% reported having been previously screened.

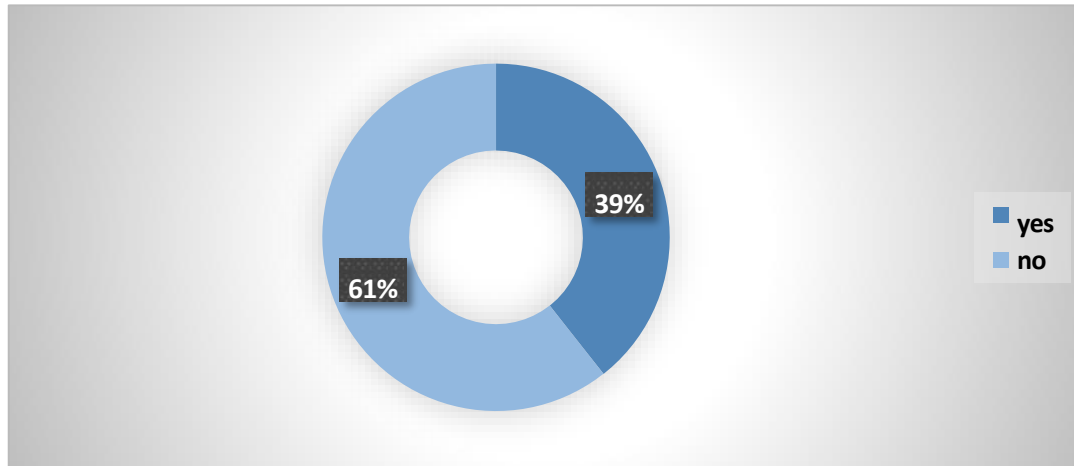


Figure 30: Distribution of patients based on their history of colorectal cancer screening.

20. Type of screening

the screening methods used by patients who had undergone previous screening.

Colonoscopy is clearly the most common screening method, used by 84.6% of patients. In contrast, the immunological test (fecal occult blood test) was used by only 14.2% of participants.

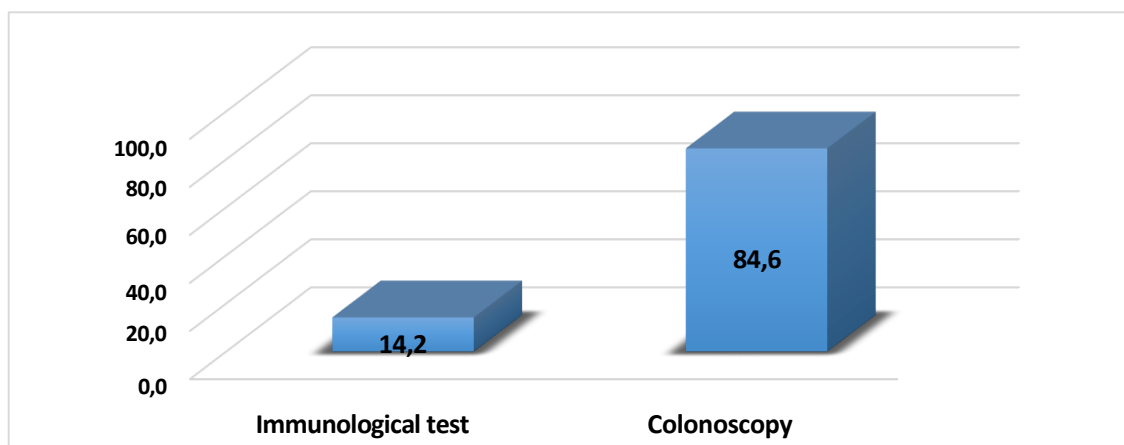


Figure 31: A Comparison of the Use of Immunochemical Testing and Colonoscopy in Screening

21. TNM stage at diagnosis

The distribution of patients according to TNM classification stages at initial diagnosis.

The results reveal a predominance of advanced stages. Indeed, the majority of patients are diagnosed at Stage III (38.3%) and Stage IV (25.9%), meaning that for more than 64% of the sample, the disease has already spread to the lymph nodes or has distant metastases. Early stages, namely Stage II (23.5%) and Stage I (12.3%), are significantly less common.

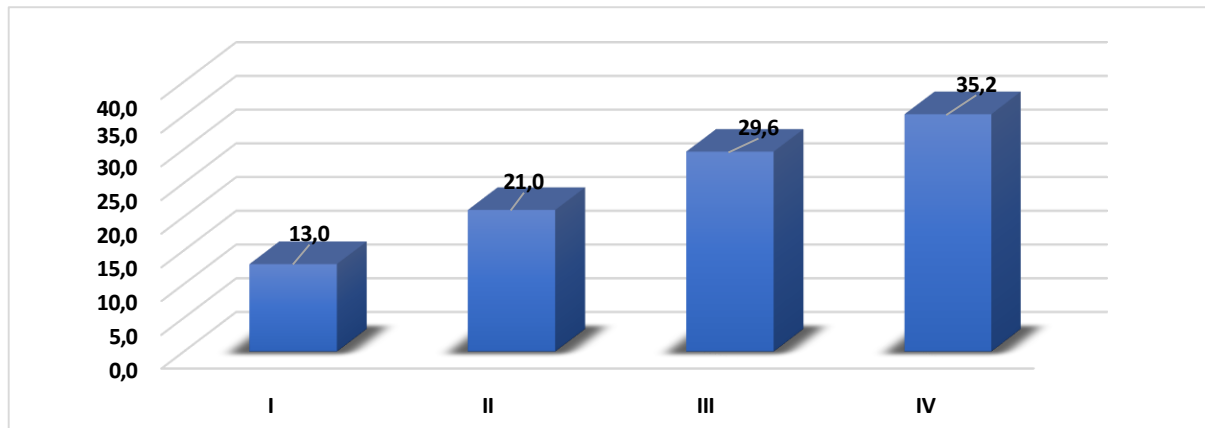


Figure 32: Assessment of Tumor Extent (TNM Classification)

22. The presence of metastases in patients

The presence of metastases at the time of diagnosis was assessed in our study population. The results show that 19.1% of patients already had distant metastases at initial presentation, while 79.6% had no metastatic spread at the time of diagnosis.

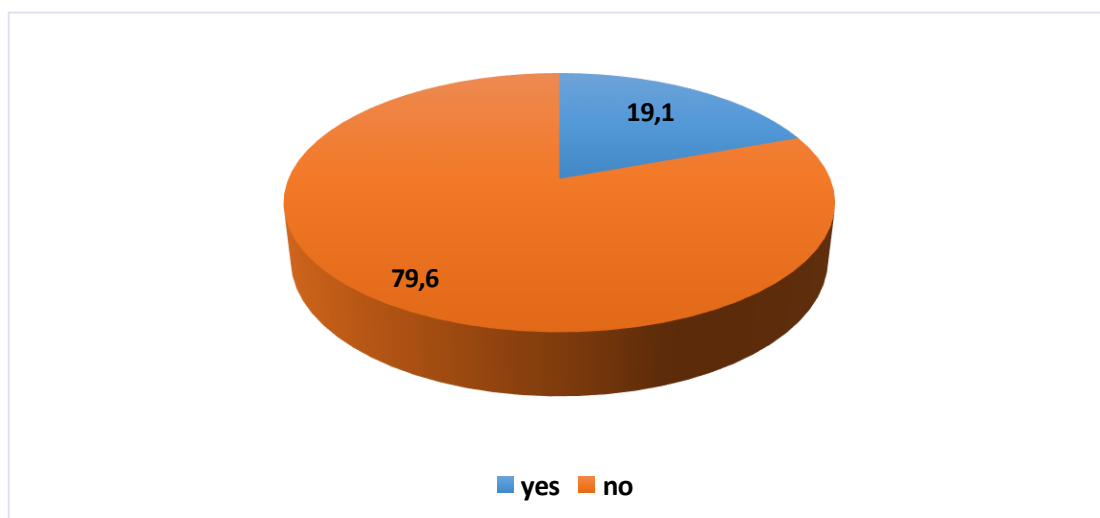


Figure 33: Prevalence of metastases at the time of diagnosis in patients

23. Location of metastases

We observed, based on the statistical analysis of our study population, that the majority of patients (80.2%) had no metastases at the time of diagnosis. However, 19.8% of cases presented with distant metastatic spread. Among metastatic sites, the liver was the most frequently affected organ (8.6%), followed by multiple-site involvement (4.9%) and lung metastases (4.3%), while other locations were rare (0.6%).

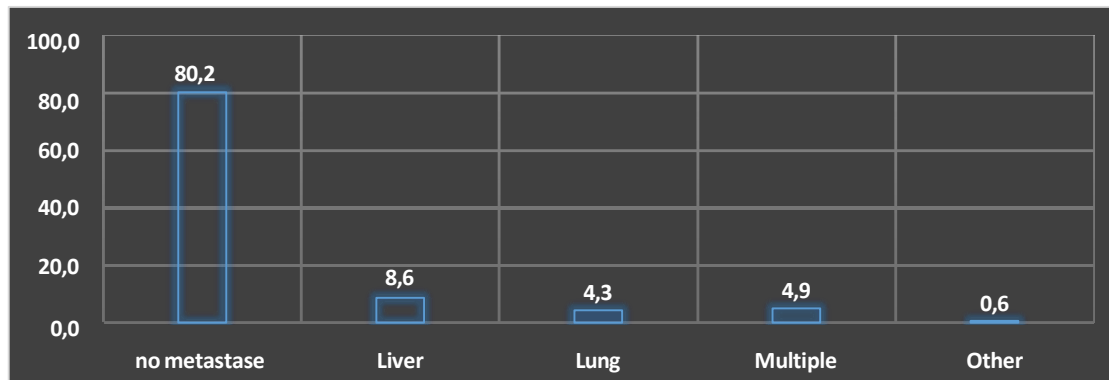


Figure 34: Distribution of metastatic sites in patients with colorectal cancer.

24. Anatomical location of the tumor

The distribution of colorectal tumors in our study demonstrated a predominance of rectal involvement, with the rectum representing the most common tumor site and accounting for 44.4% of all cases. Concerning colonic localizations, tumors were more frequently observed in the left colon (30.9%), while the right colon and the transverse colon were less commonly affected, representing 15.4% and 4.9% of cases, respectively. Furthermore, synchronous multiple tumor localizations were identified in 3.1% of the patients, indicating the presence of more than one primary tumor site at the time of diagnosis.

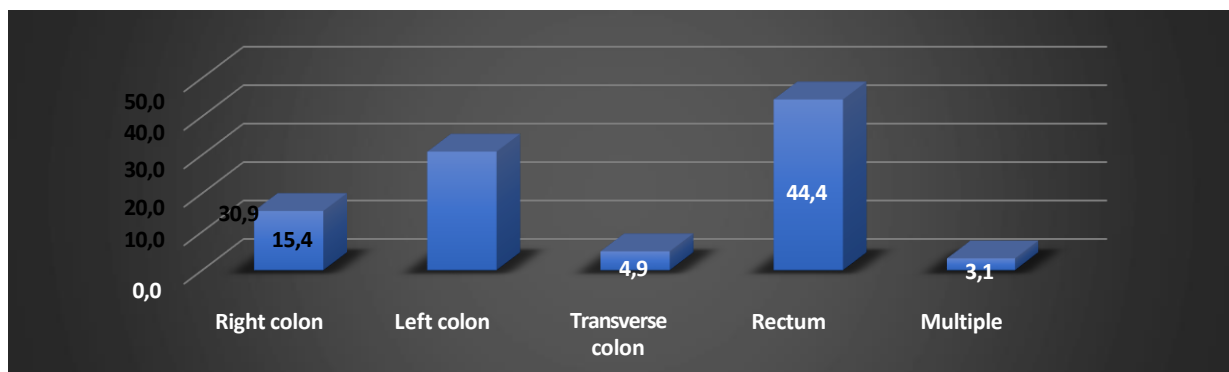


Figure 35: Distribution of patients according to the anatomical location of the tumor

ii. Comparison between the control group (40 healthy subjects) and colorectal cancer patients (162 cases)

The comparative analysis between the 40 healthy subjects and the 162 colorectal cancer patients revealed several significant differences. Among colorectal cancer patients, smoking was more frequent and significantly associated with low physical activity ($r = -0.429$; $p < 0.001$). Similarly, processed meat consumption was inversely correlated with regular physical activity ($r = -0.188$; $p = 0.017$), reflecting an accumulation of behavioral risk factors among patients compared to the control group.

Regarding protective dietary habits, a significant positive correlation was observed between fresh fruit consumption and green vegetable intake ($r = 0.261$; $p = 0.001$), as well as between fruit consumption and the intake of polyphenol-rich beverages such as tea and coffee ($r = 0.269$; $p = 0.001$). A strong association was also found between green vegetable consumption and polyphenol-rich beverage intake ($r = 0.667$; $p < 0.001$), habits more frequently observed among healthy subjects.

From a medical perspective, chronic inflammatory bowel diseases were significantly associated with a personal history of colorectal polyps ($r = 0.256$; $p = 0.001$). A positive association was also identified between a history of polyps and previous colorectal cancer screening ($r = 0.209$; $p = 0.008$). Furthermore, low dietary fiber intake was correlated with vitamin D deficiency ($r = 0.165$; $p = 0.037$), while a positive correlation was observed between a history of anemia and vitamin D deficiency ($r = 0.240$; $p = 0.002$).

Finally, from a prognostic perspective, TNM stage was strongly associated with the presence of metastases ($r = -0.482$; $p < 0.001$), and tumor location was correlated with the duration of symptoms before medical consultation ($r = 0.237$; $p = 0.003$). Chronic stress was also associated with the type of screening ($r = 0.204$; $p = 0.010$), the presence of metastases ($r = -0.197$; $p = 0.012$), and metastatic localization ($r = 0.182$; $p = 0.021$). (see the table)

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Table 4: Significant Correlations between Study Variables in Colorectal Cancer Patient

Category	Variables	Correlation (r)	p-value
Sociodemographic	Age – Employment status	0.581	<0.001
Sociodemographic	Gender – Physical activity	0.659	<0.001
Sociodemographic	Gender – Smoking	-0.584	<0.001
Medical history	Inflammatory bowel disease – Colorectal polyps	0.256	0.001
Medical history	Polyps – Previous screening	0.209	0.008
Diet	Fruit – Vegetables	0.261	0.001
Diet	Fruit – Tea/coffee/herbal drinks	0.269	0.001
Diet	Vegetables – Tea/coffee/herbal drinks	0.667	<0.001
Lifestyle	Smoking – Physical activity	-0.429	<0.001
Lifestyle	Processed meat – Physical activity	-0.188	0.017
Clinical	TNM stage – Metastasis presence	-0.482	<0.001
Clinical	Symptoms delay – Tumor characteristics	0.237	0.003
Psychosocial	Chronic stress – Clinical factors	0.182–0.204	0.010–0.021

iii. Statistical Associations Based on p-Value Analysis

The inferential statistical analysis (Chi-square test and independent samples t-test) revealed a heterogeneous pattern of associations between colorectal cancer status and the investigated variables, reflecting the multifactorial nature of the disease.

1) Non-significant associations

No statistically significant association was observed between colorectal cancer and gender ($p = 0.926$), indicating that sex distribution did not differ meaningfully between groups. Similarly, no significant relationships were found for red meat consumption ($p = 0.565$), green vegetable intake ($p = 0.230$), high-fiber food consumption ($p = 0.090$), tea/coffee intake ($p = 0.381$), history of anemia ($p = 0.389$), and the usual method of cooking meat ($p = 0.092$). Although some of these variables showed borderline tendencies, they did not reach statistical significance at the 5% threshold.

2) Socio-demographic and clinical characteristics

A highly significant association was identified between colorectal cancer and age ($p < 0.001$), confirming a clear age-related difference between patients and controls, with older age being more represented in the cancer group. Employment status was also significantly associated with disease occurrence ($p = 0.002$), suggesting potential differences in occupational distribution between groups.

3) Medical and genetic risk factors

Strong statistically significant associations were observed for key established risk factors, including chronic inflammatory bowel diseases ($p < 0.001$), personal history of colorectal polyps or tumors ($p < 0.001$), family history of colorectal cancer ($p < 0.001$), and overweight/obesity ($\text{BMI} \geq 25 \text{ kg/m}^2$) ($p < 0.001$). These findings reinforce the role of inflammation, genetic predisposition, and metabolic status in colorectal carcinogenesis. Vitamin D deficiency was also significantly associated with colorectal cancer ($p = 0.001$), suggesting a possible link with nutritional or immunological mechanisms.

4) Lifestyle and dietary behaviors

Behavioral factors showed strong associations with colorectal cancer. Smoking ($p < 0.001$), low physical activity ($p < 0.001$), and chronic stress ($p < 0.001$) were significantly more prevalent among cases, highlighting the clustering of unhealthy lifestyle behaviors in the cancer group. Regarding diet, significant associations were found with processed meat consumption ($p < 0.001$), frozen meat consumption ($p < 0.001$), fresh fruit intake ($p < 0.001$), fish consumption ($p < 0.001$), and fermented dairy product consumption ($p = 0.047$). These results suggest a combined effect of both protective (fruits, fish) and risk-related dietary patterns (processed meats).

5) Clinical presentation and disease progression

Clinically, colorectal cancer was significantly associated with the presence of pre-diagnostic symptoms ($p < 0.001$) and delayed medical consultation ($p < 0.001$), indicating that symptomatic presentation is frequent and often associated with late diagnosis.

A strong association was also observed with previous colorectal cancer screening status ($p < 0.001$) and screening type ($p < 0.001$), suggesting differences in access or adherence to screening strategies.

Disease severity markers were significantly associated with cancer status, including TNM stage at diagnosis ($p < 0.001$) and presence of metastases ($p < 0.001$). Metastatic localization showed a statistically significant association ($p = 0.027$), while tumor anatomical location was also highly significant ($p < 0.001$), indicating heterogeneity in tumor distribution and dissemination patterns.

Finally, place of residence was significantly associated with colorectal cancer ($p < 0.001$), suggesting potential geographic or healthcare access disparities influencing diagnosis patterns.

6) Overall interpretation

Collectively, these results demonstrate that colorectal cancer in this population is not linked to a single determinant but rather results from the interaction of demographic susceptibility, metabolic and genetic predisposition, lifestyle behaviors, and healthcare access factors, all contributing to disease onset and progression.

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Table 5: Global summary of association tests between colorectal cancer and studied variables

Variable	Statistical test	χ^2 / t value	df	p-value	Interpretation
Sex	Chi-square	0.009	1	0.926	Not significant
Age	t-test	5.107	208	< 0.001	Significant
Employment status	Chi-square	12.143	2	0.002	Significant
Inflammatory bowel disease (IBD)	Chi-square	29.447	1	< 0.001	Significant
Colorectal polyps	Chi-square	61.979	1	< 0.001	Significant
BMI (≥ 25 kg/m ²)	Chi-square	23.864	1	< 0.001	Significant
Family history of CRC	Chi-square	13.125	1	< 0.001	Significant
Red meat consumption	Chi-square	13.125	1	0.565	Not significant
Processed meat consumption	Chi-square	17.395	2	< 0.001	Significant
Frozen meat consumption	Chi-square	85.817	3	< 0.001	Significant
Fresh fruit intake	Chi-square	34.968	2	< 0.001	Significant
Green vegetable intake	Chi-square	2.938	2		Not significant
Fiber intake	Chi-square	4.826	2		Not significant
Fish consumption	Chi-square	34.239	2	< 0.001	Significant
Fermented dairy products	Chi-square	3.961	1		Significant
Smoking	Chi-square	21.133	2	< 0.001	Significant
Chronic stress	Chi-square	69.485	3	< 0.001	Significant

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Pre-diagnostic symptoms	Chi-square	210.000	7	< 0.001	Significant
Delay before consultation	Chi-square	210.000	3	< 0.001	Significant
Previous CRC screening	Chi-square	28.125	1	< 0.001	Significant
TNM stage	Chi-square	210.000	4	< 0.001	Significant
Metastasis presence	Chi-square	210.000	2	< 0.001	Significant
Metastasis location	Chi-square	10.938	4	0.027	Significant
Tumor location	Chi-square	210.000	5	< 0.001	Significant
Anemia	Chi-square	0.743	1	0.389	Not significant

Discussion

Among the 162 patients diagnosed with colorectal cancer included in our study, a slight male predominance was observed, with 31 males (51.7%) compared to 29 females (48.3%), resulting in a sex ratio close to unity (1.06). This finding is consistent with the study by Abid *et al.* (2014), who also reported a near-equal sex distribution with a sex ratio of approximately 1.1. However, it contrasts with data from Western literature, where a more pronounced male predominance is usually described, with sex ratios ranging from 1.5 to 2 (Barth and Leclercq, 1997). This discrepancy may be explained by geographical, environmental, and lifestyle differences between populations studied.

Although colorectal cancer is generally reported in the literature to show a slight male predominance, our findings demonstrate an almost equal distribution between males and females, suggesting a near parity in incidence. This pattern is consistent with the study of Abid *et al.* (2014), who also reported a balanced sex distribution. However, it differs from data reported in Western populations, where a clearer male predominance has been described, with sex ratios ranging from 1.5 to 2 (Barth and Leclercq, 1997). These discrepancies may be explained by differences in lifestyle exposure, hormonal influences, and regional variations in risk factor distribution.

The results of our study indicate that patients with colorectal cancer were predominantly older adults, with a considerable proportion being retired or unemployed. This age distribution is in line with the well-established epidemiological profile of colorectal cancer, which is known to be more frequent in older populations. Similar observations have been reported in several studies, including those by van Muijen *et al.* (2013), de Boer *et al.* (2009), and Mehnert (2011), which consistently demonstrated that colorectal cancer primarily affects elderly individuals and is often associated with reduced occupational activity at the time of diagnosis.

These findings reinforce the age-dependent nature of colorectal cancer and highlight its significant socio-professional impact, as disease onset frequently coincides with retirement or work incapacity. Overall, our results are consistent with the existing literature and further support the role of aging as a major determinant in colorectal cancer epidemiology.

Regarding inflammatory conditions, the high prevalence observed in our study (46%) confirms the strong association between chronic intestinal inflammation and colorectal carcinogenesis. Similar findings have been reported in previous studies, where inflammatory bowel diseases

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Were identified as a major risk factor for colorectal cancer due to persistent mucosal injury and continuous regenerative processes (Itzkowitz and Yio, 2004; Jess *et al.*, 2012). Chronic inflammation is known to promote DNA damage, oxidative stress, and dysregulated cell proliferation, thereby increasing malignant transformation risk. Our results are therefore in agreement with the established literature highlighting inflammation as a key driver in colorectal cancer development.

The majority of patients in our study (64%) had a personal history of colorectal polyps, while 36% had no such history. These findings reinforce the importance of the adenoma–carcinoma sequence, according to which colorectal cancer frequently develops from pre-existing adenomatous polyps. Our results are consistent with the work of Vogelstein *et al.* (1988), who demonstrated the central role of adenomatous polyps in colorectal carcinogenesis. Similarly, Winawer *et al.* (1993) showed that polypectomy significantly reduces the risk of colorectal cancer.

A high consumption of red meat was also observed in our study population. Indeed, 78% of patients consumed red meat once or twice per week, while 22% reported consumption three times or more per week. This high frequency may be associated with an increased risk of colorectal cancer. Our findings are comparable to those reported by Cross *et al.* (2010), who demonstrated that regular red meat consumption is significantly associated with an increased risk of colorectal cancer, particularly in individuals consuming meat cooked at high temperatures.

Similarly, Chan *et al.* (2011), in a meta-analysis of prospective studies, showed that high red meat intake increases colorectal cancer risk due to the formation of carcinogenic compounds such as heterocyclic amines and polycyclic aromatic hydrocarbons.

Our results are also consistent with those of Bouvard *et al.* (2015), published by the International Agency for Research on Cancer (IARC), which classified red meat as “probably carcinogenic to humans.” The authors highlighted that heme iron promotes oxidative stress and DNA damage in colonic cells.

Furthermore, Norat *et al.* (2005) reported that a diet high in red meat and low in dietary fiber promotes intestinal inflammation and increases the risk of malignant transformation. This observation is in agreement with our study, in which most patients reported frequent red meat consumption.

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Frozen meat consumption observed in our study is not considered a direct carcinogenic factor. However, it may be associated with dietary patterns that increase colorectal cancer risk. Improper storage or repeated freezing–thawing cycles may reduce nutritional quality and promote lipid oxidation (Bouvard *et al.*, 2015). Moreover, such products are often part of diets rich in processed foods and high-temperature cooking methods, which can generate mutagenic compounds such as heterocyclic amines and polycyclic aromatic hydrocarbons (Cross & Sinha, 2004). High consumption of frozen foods may also reflect a low intake of dietary fiber, thereby reducing intestinal protective effects.

Thus, although frozen meat is not directly implicated, the associated dietary habits may contribute to colorectal cancer risk, as highlighted by the World Cancer Research Fund International.

Our study also showed a high consumption of grilled and fried foods among patients, which may represent a potential risk factor for colorectal cancer. High-temperature cooking of meat promotes the formation of heterocyclic amines (HCA) and polycyclic aromatic hydrocarbons (PAH), both of which are recognized mutagenic agents affecting colonic mucosal cells (Cross & Sinha, 2004).

These findings are consistent with those of Sinha *et al.* (1999), who reported a positive association between frequent consumption of grilled meat and colorectal cancer risk. Similarly, Cantwell *et al.* (2004) showed that high exposure to PAHs and HCAs increases DNA mutation risk in colonic tissue.

In addition, Bouvard *et al.* (2015), on behalf of the International Agency for Research on Cancer, emphasized that dietary factors related to processed meats and cooking methods may contribute to colorectal carcinogenesis. Our results support these findings, as the high intake of fried and grilled foods observed in our population suggests increased exposure to these carcinogenic compounds.

Thus, our findings confirm the literature indicating that cooking practices represent an important environmental factor in colorectal carcinogenesis.

Although fruits are known for their protective effects due to their richness in dietary fiber, antioxidants, and polyphenols, their consumption alone is not always sufficient to prevent colorectal cancer. In our study, despite relatively high fruit intake, patients still developed the disease, suggesting the involvement of additional risk factors such as high consumption of red

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and processed meats, high-temperature cooking methods, family history, lifestyle patterns, and genetic susceptibility.

Our findings are consistent with those of Aune *et al.* (2011), who reported that fruit and dietary fiber intake are associated with a reduced risk of colorectal cancer, although they do not provide complete protection. Similarly, the World Cancer Research Fund International emphasizes that colorectal cancer is a multifactorial disease influenced by a combination of dietary, environmental, and lifestyle factors. Therefore, despite the protective role of fruit consumption, its effect remains limited in the presence of other carcinogenic exposures in patients' lifestyles.

The majority of patients (86%) reported daily consumption of green vegetables, despite the presence of colorectal cancer, suggesting no clear protective association within our population. These findings are in line with Aune *et al.* (2011), who highlighted that the protective effect of vegetables is strongly dependent on overall dietary patterns and lifestyle factors, indicating that other risk determinants may play a more dominant role in disease development.

The high consumption of dairy products observed among our patients primarily reflects local dietary habits. However, excessive intake of full-fat dairy products may be linked to colorectal cancer risk through increased insulin-like growth factor 1 (IGF-1) activity, which promotes cellular proliferation, as well as through pro-inflammatory effects of saturated fats. This nutritional pattern is often associated with other risk factors such as low fiber intake and high consumption of processed meats. Our results are consistent with those of Norat and Riboli (2003) and Turner and Lloyd (2011), who reported an association between animal fats, certain dairy products, and increased colorectal cancer risk through inflammatory and oxidative mechanisms. In contrast, the meta-analysis by Aune *et al.* (2012) highlighted a potential protective role of calcium and fermented dairy products against colorectal carcinogenesis. These discrepancies suggest that the impact of dairy products depends on their type, quantity, and the overall dietary context.

A very high prevalence of tea and coffee consumption (96%) was observed in our study, which may be explained by sociocultural habits, as these beverages are widely consumed daily in North African and Mediterranean populations. Similar findings were reported by Dik *et al.* (2014), who observed high coffee consumption among study participants, attributing it to habitual dietary behavior and the stimulant and digestive properties of coffee. Likewise, Sinha *et al.* (2001) reported high consumption levels of tea and coffee in adult urban populations.

Several studies suggest that tea and coffee may exert protective effects against colorectal cancer due to their high content of polyphenols, flavonoids, and other antioxidant compounds. These bioactive molecules may reduce oxidative stress and chronic inflammation, both of which are involved in colorectal carcinogenesis. Zhang *et al.* (2015) demonstrated that tea polyphenols could inhibit tumor cell proliferation and reduce oxidative damage in colonic mucosa. Additionally, coffee contains bioactive compounds such as chlorogenic acids and diterpenes, which possess anti-inflammatory and antioxidant properties.

Among the 162 colorectal cancer patients included in our study, a high prevalence of chronic stress was observed. Indeed, 61.1% of participants reported high stress levels and 32.1% moderate stress, indicating that more than 93% of patients experienced significant psychological stress. These findings are consistent with Yan *et al.* (2023), who reported that chronic stress is common among patients with gastrointestinal cancers and may contribute to disease progression.

Chronic stress may promote colorectal carcinogenesis through multiple biological pathways, including increased cortisol and catecholamine secretion, leading to chronic inflammation, immune suppression, and enhanced oxidative stress, thereby facilitating tumor cell proliferation. Baritaki *et al.* (2019) also demonstrated that chronic stress contributes to intestinal inflammation and colorectal cancer progression.

Our results show that colorectal cancer is most often diagnosed at a symptomatic stage. The most frequent clinical manifestations were bowel habit disturbances, particularly chronic constipation (29.6%). From a clinical perspective, chronic constipation may suggest partial luminal obstruction by the tumor, often associated with distal colorectal lesions. Fatigue may reflect chronic occult anemia due to microscopic tumor bleeding, which is not always perceived by patients, in contrast to the low proportion reporting overt rectal bleeding (6.2%). The nonspecific nature of these symptoms often leads to delayed medical consultation and underestimation in early disease stages. These findings emphasize the importance of early screening in cases of persistent changes in bowel habits to prevent late-stage diagnosis. Our results are consistent with those of Brenner *et al.* (2014), who highlighted the role of nonspecific early symptoms in delayed colorectal cancer diagnosis.

Results & discussion

Our study highlights a significant delay in medical consultation among patients with colorectal cancer. Only 29.6% of patients consulted within less than 3 months after symptom onset, while 38.9% sought medical attention between 3 and 6 months, and 30.2% after more than 6 months, indicating that nearly 70% of patients experienced a diagnostic delay exceeding 3 months. These findings are consistent with those of Richards *et al.* (1999) and Mitchell *et al.* (2008), who also reported prolonged diagnostic delays largely related to the nonspecific nature of early symptoms and their underestimation by patients. This delay may be explained by symptom ambiguity, normalization of digestive disorders, sociocultural barriers such as fear of diagnosis and self-medication, as well as limited awareness of colorectal cancer screening.

Our results also show a low uptake of colorectal cancer screening, as 61% of participants had never undergone screening, compared with only 39% who had been screened. These findings are in line with previous studies reporting poor participation in screening programs, mainly due to lack of awareness, limited access to healthcare, and absence of organized screening strategies (von Karsa *et al.*, 2013; Arnold *et al.*, 2017). Overall, these results emphasize the urgent need to strengthen awareness campaigns and improve screening coverage to enable earlier detection.

The TNM stage distribution at diagnosis demonstrates a predominance of advanced disease in our cohort. Indeed, stage III (38.3%) and stage IV (25.9%) together account for more than 64% of cases, while early stages remain less frequent (stage II: 23.5%; stage I: 12.3%). These findings are consistent with the literature, which reports a high proportion of late-stage diagnoses, particularly in settings with low screening uptake and delayed consultation (Siegel *et al.*, 2020; Arnold *et al.*, 2017). This pattern is mainly attributed to late disease detection and the nonspecific nature of early symptoms.

The presence of metastases in 19.1% of patients at diagnosis indicates that nearly one in five patients already presented with stage IV disease at initial presentation. This observation is consistent with the TNM distribution, confirming a substantial proportion of advanced-stage cases. In colorectal cancer, metastatic spread—most commonly to the liver and lungs—significantly limits curative treatment options and often necessitates systemic therapy rather than surgical management. These results are consistent with large epidemiological studies, where Siegel *et al.* (2020) reported that approximately one-fifth of colorectal cancer cases are diagnosed at metastatic stage, particularly in populations with limited screening. Similarly, Arnold *et al.* (2017) identified delayed diagnosis as a major global determinant of stage IV presentation.

Results & discussion

Regarding metastatic localization, our findings align with the literature identifying the liver as the most frequent site of metastasis in colorectal cancer, due to direct portal venous drainage from the colorectal region. Vatandoust *et al.* (2015) and Van Cutsem *et al.* (2016) similarly reported hepatic metastases as the predominant site, followed by pulmonary and peritoneal involvement. From a pathophysiological perspective, this distribution is explained by portal circulation, which facilitates early dissemination of tumor cells to the liver, the first filtration organ. Pulmonary metastases generally occur later as part of systemic spread.

From a clinical perspective, the high prevalence of rectal cancer (44.4%) and left-sided colon cancer (30.9%) may explain the frequent bowel habit disturbances observed in our patients, particularly chronic constipation reported in 29.6% of cases. Distal tumors are more likely to cause luminal narrowing, resulting in early obstructive symptoms. These findings are consistent with the literature, which indicates that the rectum and left colon remain the most common sites of colorectal carcinogenesis. The accessibility of these lesions through physical examination or endoscopy underscores the importance of early clinical evaluation when initial symptoms appear.

Finally, the higher concentration of cases in Oued Rhiou may be attributed to greater population density and better access to healthcare services and diagnostic facilities.

In contrast, the lower frequency of cases in peripheral regions likely reflects reduced healthcare accessibility and lower population density.

These geographical disparities in healthcare access may contribute to delayed diagnosis and a higher proportion of advanced TNM stages, as observed in our study.

Conclusion

Colorectal cancer (CRC) represents a major public health issue worldwide and in Algeria due to its increasing incidence and high mortality rate. The development of this disease results from a complex interaction between genetic, environmental, and behavioral factors. Advanced age, family history, chronic inflammatory bowel diseases, unhealthy dietary habits, obesity, smoking, alcohol consumption, and physical inactivity are among the main factors associated with an increased risk of CRC.

The results of our study highlighted several factors significantly associated with colorectal cancer. Age, employment status, inflammatory bowel disease, colorectal polyps, obesity, and family history of CRC showed strong statistical associations with the disease. Regarding dietary habits, the consumption of processed meat and frozen meat significantly increased the risk of CRC, while low consumption of fresh fruits and fish was also associated with this pathology. Smoking and chronic stress were identified as significant risk factors. In contrast, sex, red meat consumption, fiber intake, green vegetable consumption, and anemia showed no statistically significant association with CRC.

Our study also revealed that pre-diagnostic symptoms, delayed medical consultation, and lack of previous screening were strongly associated with colorectal cancer, emphasizing the importance of early diagnosis. Clinical and tumor-related parameters, including TNM stage, presence and location of metastases, and tumor localization, were also significantly associated with the disease.

Despite considerable progress in diagnosis and treatment, the prognosis of colorectal cancer remains closely related to the stage at diagnosis. Therefore, early screening, identification of risk factors, and adoption of a healthy lifestyle remain essential strategies to reduce the incidence and mortality associated with this disease.

In conclusion, strengthening prevention programs, improving access to screening, increasing public awareness about modifiable risk factors, and promoting healthy dietary habits and regular physical activity could contribute significantly to reducing the burden of colorectal cancer in Algeria.

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