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*To my loving **parents,***

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Abstract

NK: Natural killer.

NOS: Not Otherwise Specified.

PCPs: Primary Care Physicians.

PCR: Polymerase Chain Reaction.

PD-1: Programmed Cell Death Protein 1.

PDX-1: The homeobox duodenal pancreatic transcription factor.

SAHGEED: Algerian Society of Hepato gastro-enterology and Digestive Endoscopy.

SMAD4: Mothers against decapentaplegic homolog 4.

STAT3: Signal transducer and activator of transcription 3 genes.

T: (Tumor) the primary tumor.

TAM: Tumour-associated macrophage.

TAN: Tumor-Associated Neutrophils.

TBS: Tris-buffered saline.

TBS1: Tris-buffered saline 1.

TBS2: Tris-buffered saline 2.

TGFBR2: Transforming Growth Factor Beta Receptor 2.

Th: T-helper cells.

TILs: Tumor infiltrating lymphocytes.

TME: The tumor microenvironment.

TNF: Tumor necrosis factor.

TNM : Tumeur Node Métastas0 G[(NO)4(S)-3(: Not Other)5(wise)3(S)-3(pe)-5(c)4(ifie)3(d.)] TJETQq053

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Introduction

Introduction

Colorectal cancer (CRC), including cancer of the colon and/or rectum, is a major health challenge as it ranked as the third most frequently diagnosed cancer and the second leading cause of cancer-related deaths worldwide. In 2020, CRC accounted for around 9.4% of all cancer-related deaths. However, due to a substantial rise in diagnosed cases among the elderly, it is projected that the global incidence of CRC will more than double by 2035, with the greatest increase expected in less developed countries **(Hossain Ms et al., 2022).**

CRC holds the second position in terms of frequency among cancers in Algeria, with lung cancer being the most common in men and breast cancer being the most common in women. These statistics are based on data from the National Institute of Public Health in the year 2015 **(Laouar et Daoudi, 2016).**

CRC is a disorder that occurs exclusively in the colon or rectum and is caused by the colon's aberrant proliferation of glandular epithelial cells. There are three principal types of CRC: Sporadic, hereditary, and colitis-associated. The number of CRC cases is increasing globally day by day. Both environmental and genetic factors determine the risk of developing CRC **(Hossain Ms et al., 2022).** Furthermore, the likelihood of developing CRC in individuals with long-standing ulcerative colitis and Crohn's disease rises with age **(Triantafillidis J.K. et al., 2009)**. Numerous studies have provided evidence that various factors contribute to the risk of this disease, such as dietary and lifestyle choices, family history, and chronic inflammation. **(Edwards B.K. et al., 2010).**

The aim of this study is to carry out a histological study focusing on anatomo- pathology and to examine the various diagnostic techniques used for CRC, exploring their benefits and specificities in detecting this condition. Our research comprises a comprehensive literature review encompassing fundamental aspects of the colon and rectum (anatomy, histology, and physiology), as well as CRC (risk factors, carcinogenesis, pathological anatomy, diagnosis, treatment, and prognosis). We also investigated the diagnostic techniques employed for it in Algeria and assess the accuracy of the anatomopathological study protocol in achieving an exact diagnosis. Moreover, a retrospective statistical survey (2020-2022) in which we studied several parameters associated with this cancer was conducted. The survey focused on a population of patients from Eastern Algeria, administered at the Department of Pathological Anatomy of

CHU Iben Badis Constantine. The medical records of high-risk patients and those diagnosed with colorectal cancer (CRC) who were treated at the same department were involved. Additionally, we familiarized ourselves with various diagnostic techniques.

Literature review

Chapter I

Colorectal Cancer Presentation

1. The anatomy of the large intestine

1.1 The colon

The colon is the large intestine's central segment. It runs from the cecum to the rectum and is divided into four sections from a single point of view: the ascending colon, transverse, descending, and sigmoid **(figure 1).**

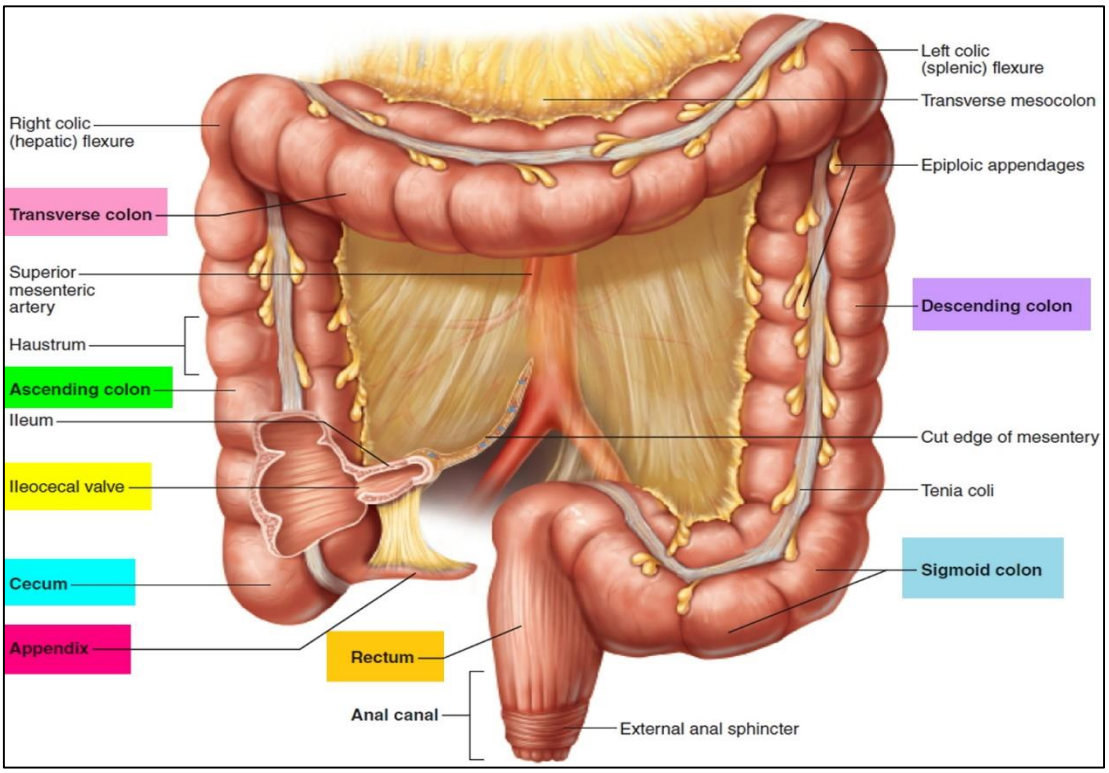

Figure1. The anatomical aspect of the colon

https://healthjade.com/large-intestine/

1.2 The rectum

The rectum is the large intestine's final segment. It is approximately 15 centimeters long and connects the colon sigmoid to the anal canal **(figure 2**), the one that opens outward through the anus. The rectum is bounded above by the recto-sigmoid junction and below by the recto-anal junction. **(Kalmogho, 2001).**

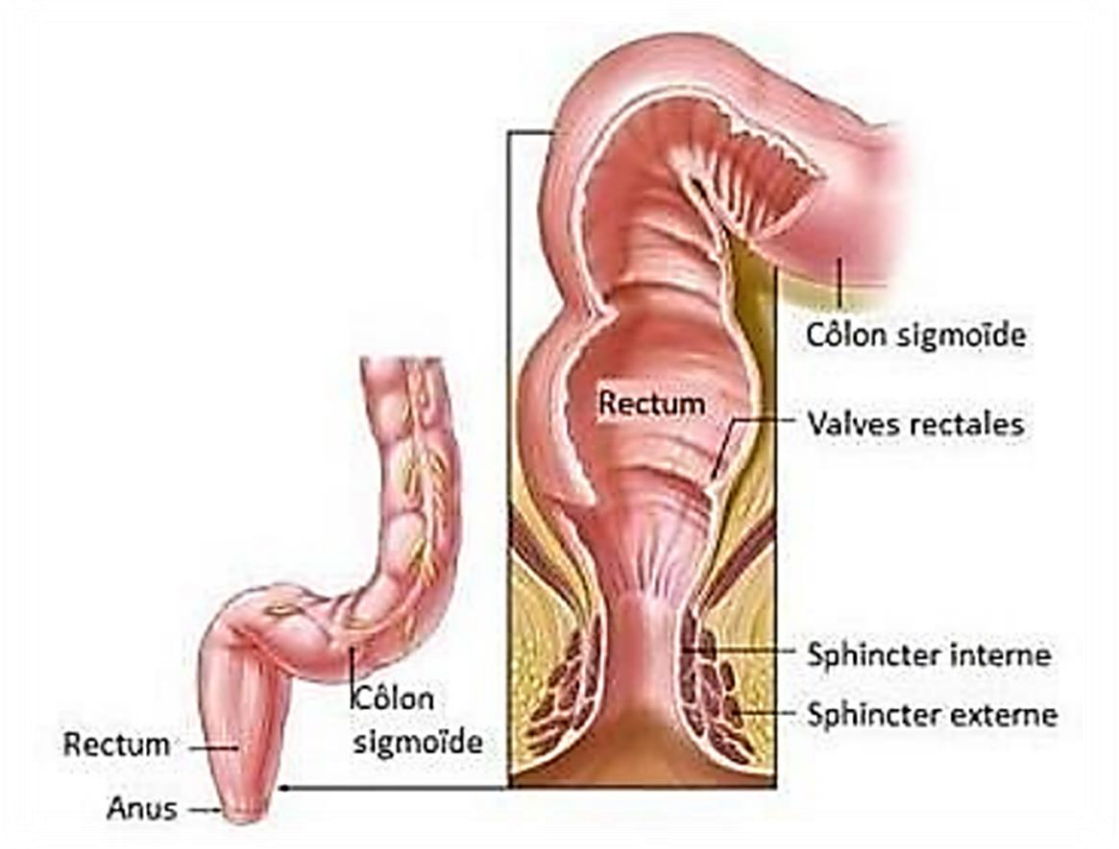

Figure 2. Rectum anatomy **(Eustache, 2001).**

2. Histology

The colorectal wall is composed of four layers. The outermost layer is the serosa or visceral peritoneum, followed by the two-layer muscular layer (an outer longitudinal layer and an inner circular layer). The submucosa lies beneath the muscular layer and is rich in blood vessels, lymphatic plexuses, and Meissner's plexus. The innermost layer is the mucosa, separated from the submucosa by the muscularis mucosae. The mucosa contains Lieberkühn glands, responsible for the secretion of mucus and enzymes, and plays a crucial role in water and electrolyte absorption **(figure. 3) (Chin et al., 2008).**

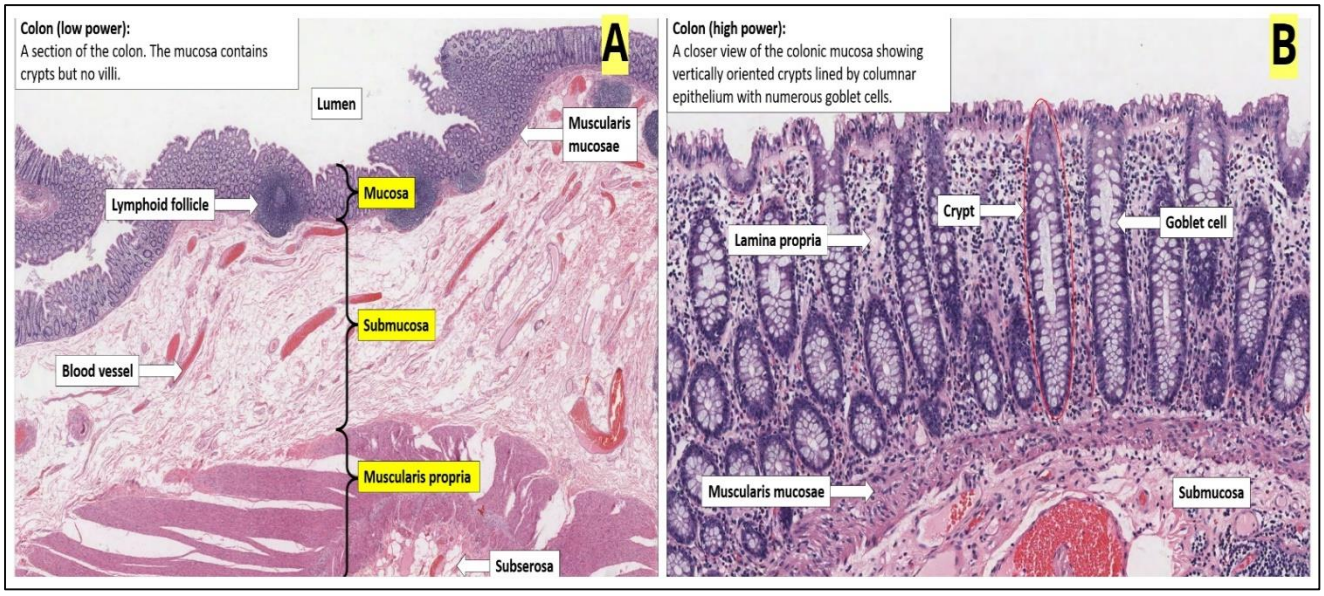

Figure 3. A) The histological appearance of colon layers**.** B) closer view of the colonic mucosa https://medicine.nus.edu.sg/pathweb/normal-histology/colon/

3. Colorectal cancer

3.1. Colorectal Cancer Presentation

Colorectal cancer (CRC) is the third most common type of cancer in oncologic pathology **(Smith RET, 2004).** Currently, it is the most common cancer in the gastrointestinal tract, representing 13% of all malignant tumors. It is considered the second most common cause of death related to cancer affecting men and women in the same manner worldwide **(Dobre M, 2015).** However, due to risk factors such as obesity, sedentarism, poor nutritional habits (high in fats and proteins), smoking, and population aging, this pathology is diagnosed more frequently in younger patients. The clinical presentation of CRC patients is determined by the location, size, and presence or absence of metastases **(Granados et al., 2017).**

CRC usually starts as a polyp in the intestinal mucosa, even so, it may additionally exist as a benign lesion called an adenoma that can transform into a malignant lesion depending on its histological presentation and size, with 60% of cases being simple adenomas and 40% being multiple adenomas. Studies demonstrated that untreated polyps cause cancer in 24% of patients **(DeVita V, 2011).** A colon polyp is a fleshy growth on the inside of the colon, it can be sessile (attached directly to the colon without a stalk) or pedunculated (attached to the colon with a stalk). Polyps are classified as non-neoplastic (harmless) or neoplastic (cancerous). **(Jayan., 2016).**

3.2. Colorectal cancer etiology

Multiple factors have been implicated in the development of CRC **(Figure 4).** It was demonstrated that individuals are at increased risk for CRC if they (or their relatives) have had cancer, a history of colon polyps, inflammatory bowel diseases, diabetes mellitus, or cholecystectomy. Lifestyle factors also play important roles in CRC etiology. Obesity, physical inactivity, cigarette smoking, alcohol consumption, and inappropriate dietary patterns (a diet low in fiber, fruits, vegetables, calcium, and dietary products and high in red and processed meat) all increase the risk of CRC. Furthermore, colorectal cancer risk is known to be influenced by the gut microbiome, age, gender, race, and socioeconomic status **(Sawicki, 2021).**

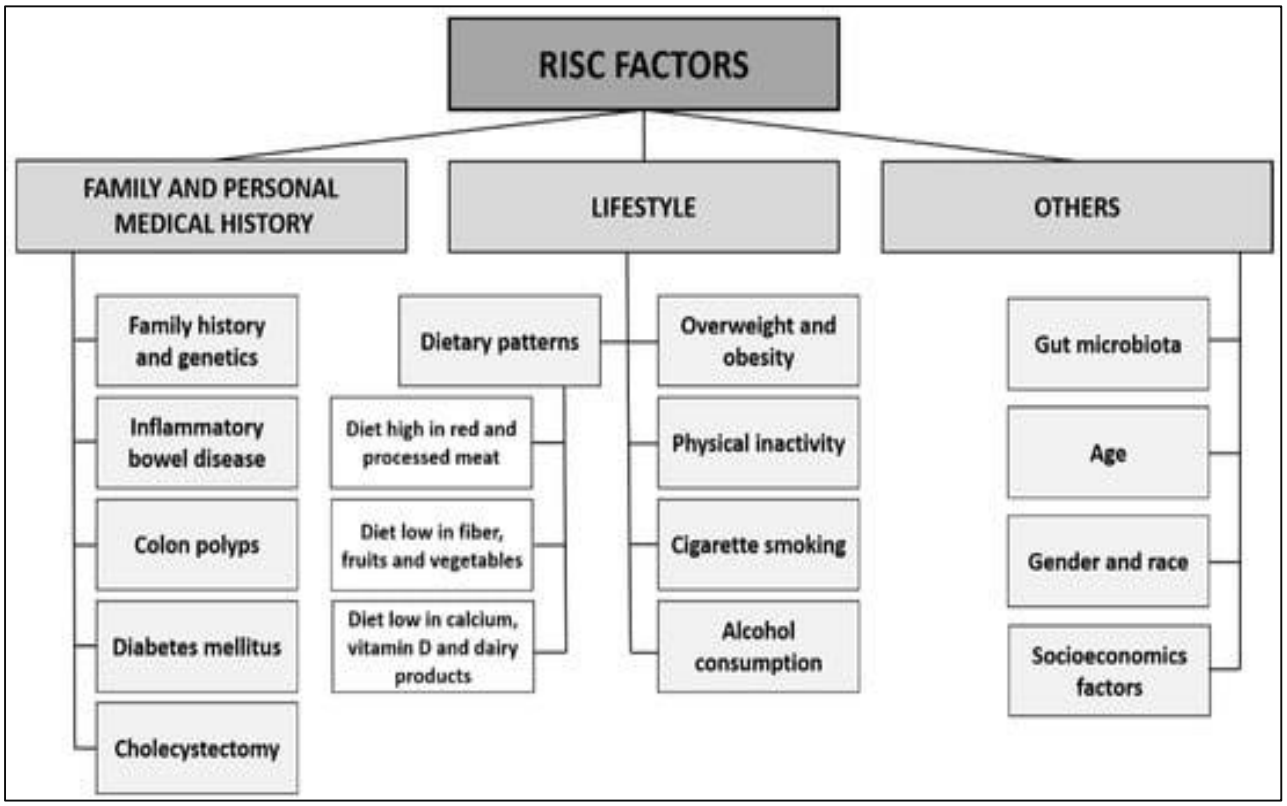

Figure 4. The main risk factors associated with colorectal cancer (Sawicki, 2021).

3.3 Pathophysiology

Cancer is defined as the uninhibited and uncontrolled growth of abnormal cells within the body's tissues, organs, or systems. Cancer risk factors can be either peripheral, such as regular exposure to hazardous chemicals, radiation, and infectious diseases, or visceral, such as abnormal cell growth caused by hormonal changes, gene mutations, and immune system dysfunction **(Harkl et al., 2007).** Individual physiology, age, and hereditary factors may all

play a role in the development of cancer. Cancer can affect any organ or tissue, including the colon, breast, prostate, bone, and blood **(A J Franke et al., 2020).** In the case of CRC, the growth and dispersal of neoplastic alterations are visible and are characterized by tumoral growth in the bowel regions of the body **(Virostko et al., 2019).** Significant alterations in the sequence of DNA are present.

3.3.1 Stages of colorectal cancer

CRC develops when epithelial cells acquire a series of genetic or epigenetic changes that enable them to be hyperproliferative **(Testa, 2018).** It is defined by the development of normal cells to hyperplastic polyps, sessile serrated adenomas, and eventually cancer **(Keum, 2019).** When an adenocarcinoma becomes invasive, it can spread to other body parts via blood and lymphatic vessels (**Figure 5**). Adenocarcinomas account for roughly 96% of all CRCs **(Pickhardt, 2013).** However, up to 18 years may pass between developing a polyp and invasive cancer. On average, it takes nine years to form metastasis **(Stryker, 1987).**

Like any other tumor or cancer, CRC is classified by stage 0 (carcinoma in situ) through stage IV (**Figure 5**). Typically, dysplastic tissue formation (tumor) occurs due to non-cancerous growth, ultimately leading to CRC development once the cells undergo multiple abnormal DNA changes. Hyperproliferation causes a (benign) polyp or adenoma to form (stage 0). Around 10% of adenomatous polyps may progress to become malignant, forming an adenocarcinoma that infiltrates the muscular propria (stage I). As the tumor grows, it invades tissues in the serosa and visceral peritoneum (stage II). If metastasis occurs in the lymphatic vessels, it progresses to stage (stage III). If it occurs in the blood vessels, it progresses to stage IV. While surgery is the standard treatment for stages II of CRC, stage III requires both surgery and adjuvant chemotherapy. Stage IV and recurrent CRC, on the other hand, necessitate surgery, chemotherapy, and targeted therapy. However, it is regrettable that there is currently no established cure for CRC **(Hossain MS, 2022).**

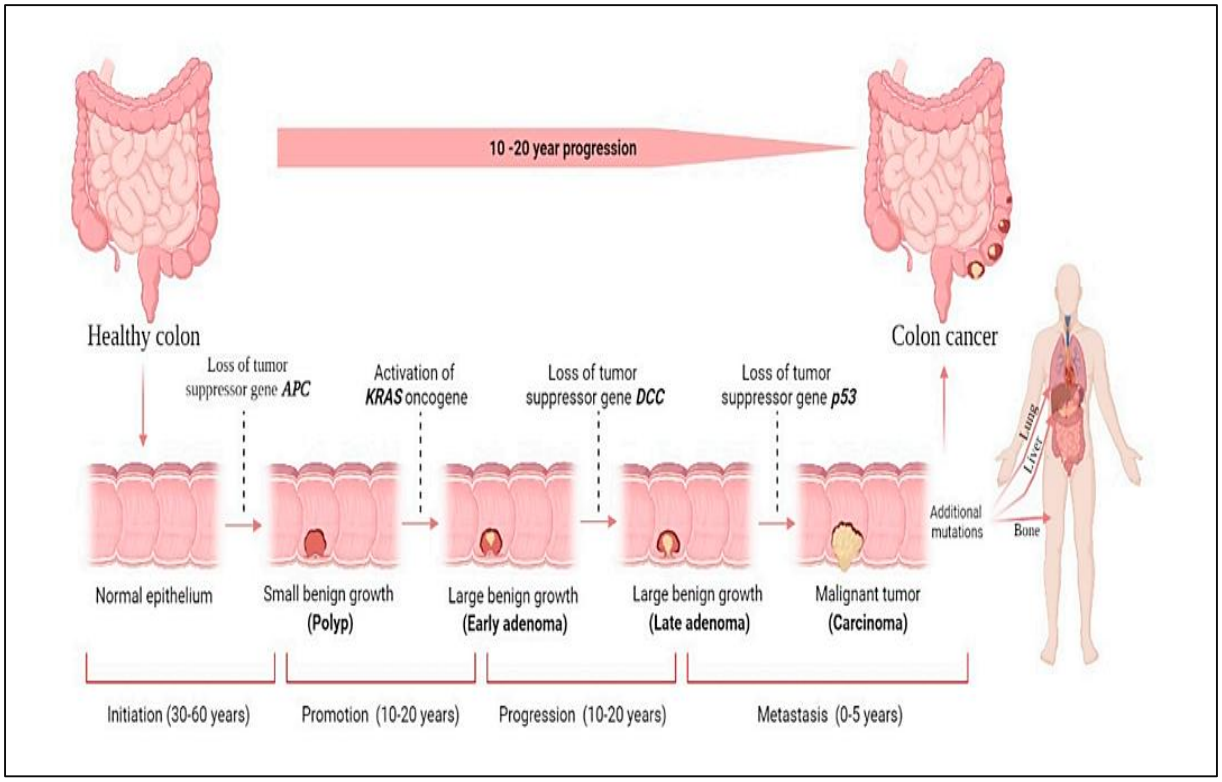

Figure 5. Colorectal cancer (CRC) stages and development. There are four stages in the development of CRC carcinogenesis: initiation, promotion, progression, and metastasis. Although it is difficult to determine the duration required for each stage, decades will likely be required to form CRC **(Hossain MS, 2022; BioRender.com accessed on 30 December 2021)**.

3.3.2 Immunopathology aspect of the disease

a- The Inflammatory environment of colorectal cancer

There are three major ways that inflammation can be linked to CRC **(figure 6).** A) chronic inflammation caused by infections, dysregulated immune responses, or environmental factors can initiate and promote tumorigenesis by inducing DNA damage or epigenetic changes, such as those caused by oxidative stress or exposure of the stem cell compartment to mutagenic. compounds due to epithelial barrier defects or constant exposure to proliferative inflammatory processes. B) tumor progression initiates an inflammatory response that is frequently pro-tumorigenic due to hypoxia-induced cell death, the epithelial barrier breakdown, and the subsequent influx of microbial products. C) similarly, therapy-induced inflammation can result in tumor-promoting inflammation as a result of the release of damage-associated molecular patterns (DAMPs) from necrotic cells **(Schmitt and Greten, 2021).**

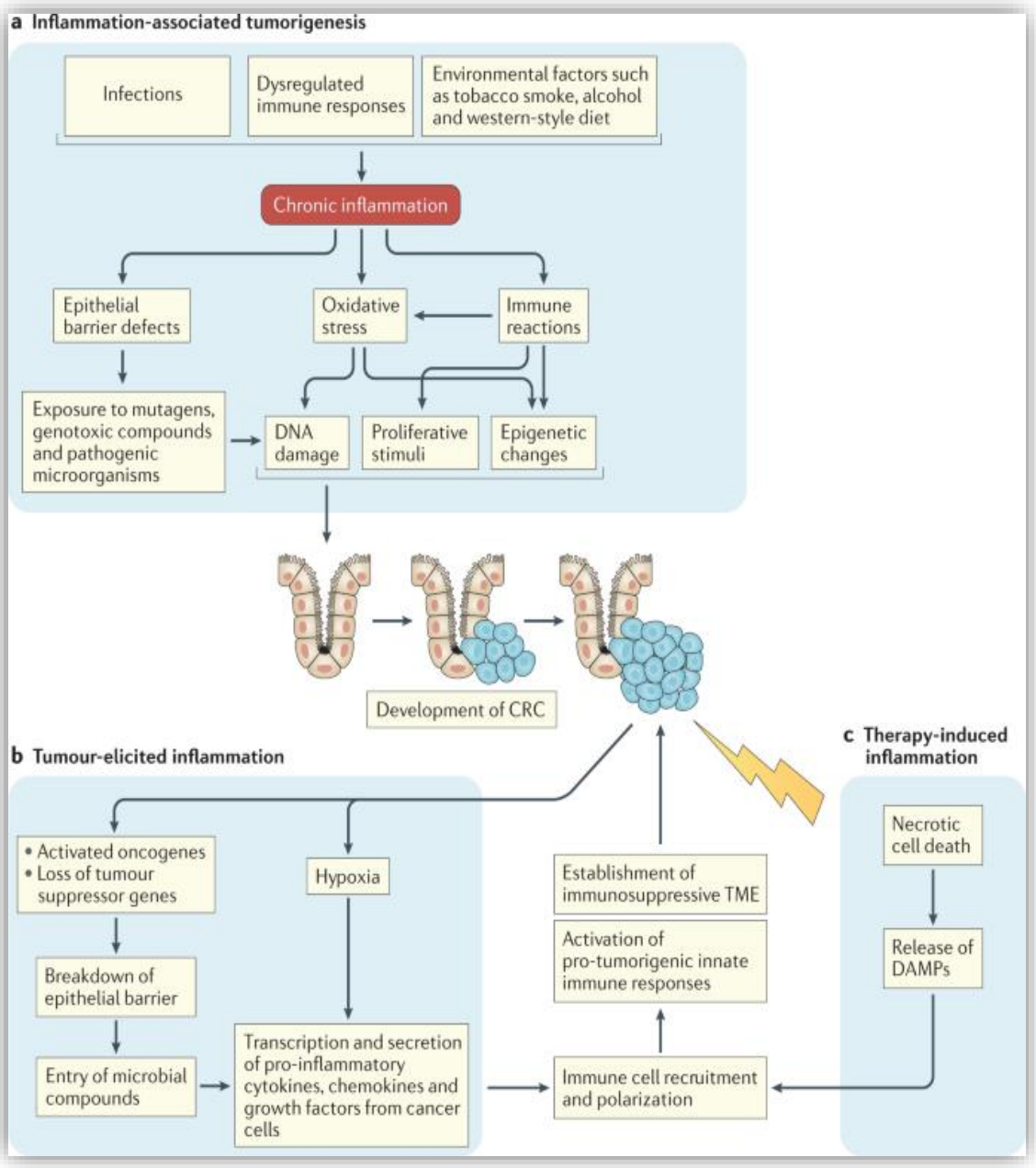

Figure 6. The figure depicts the inflammatory environment of colorectal cancer **(Schmitt and Greten, 2021).**

b- The Mechanisms of tumor initiation and promotion in colorectal cancer

Colorectal tumorigenesis requires the transformation of normal intestinal epithelial cells (IECs) via spontaneous mutation, environmental mutagens, or inflammation-induced (epigenetic changes), **(figure 7)**. The clonal expansion of these 'initiated' cells, which is fueled by mutations that cause the Hyperproliferation of APC or other genes encoding WNT pathway signaling

components, additional mutations such as KRAS, TP53, or TGFBR2, and growth stimulatory factors from the tumor microenvironment (TME) all contribute to the outgrowth of these clones into malignant tumors, a process known as tumor promotion. Additional TME mutations and modifications of these tumors can then spread to other parts of the body. Epithelial tumor tissue is constantly interacting with cells in the TME via the effects of cytokines, chemokines, and growth factors **(Schmitt and Greten, 2021).**

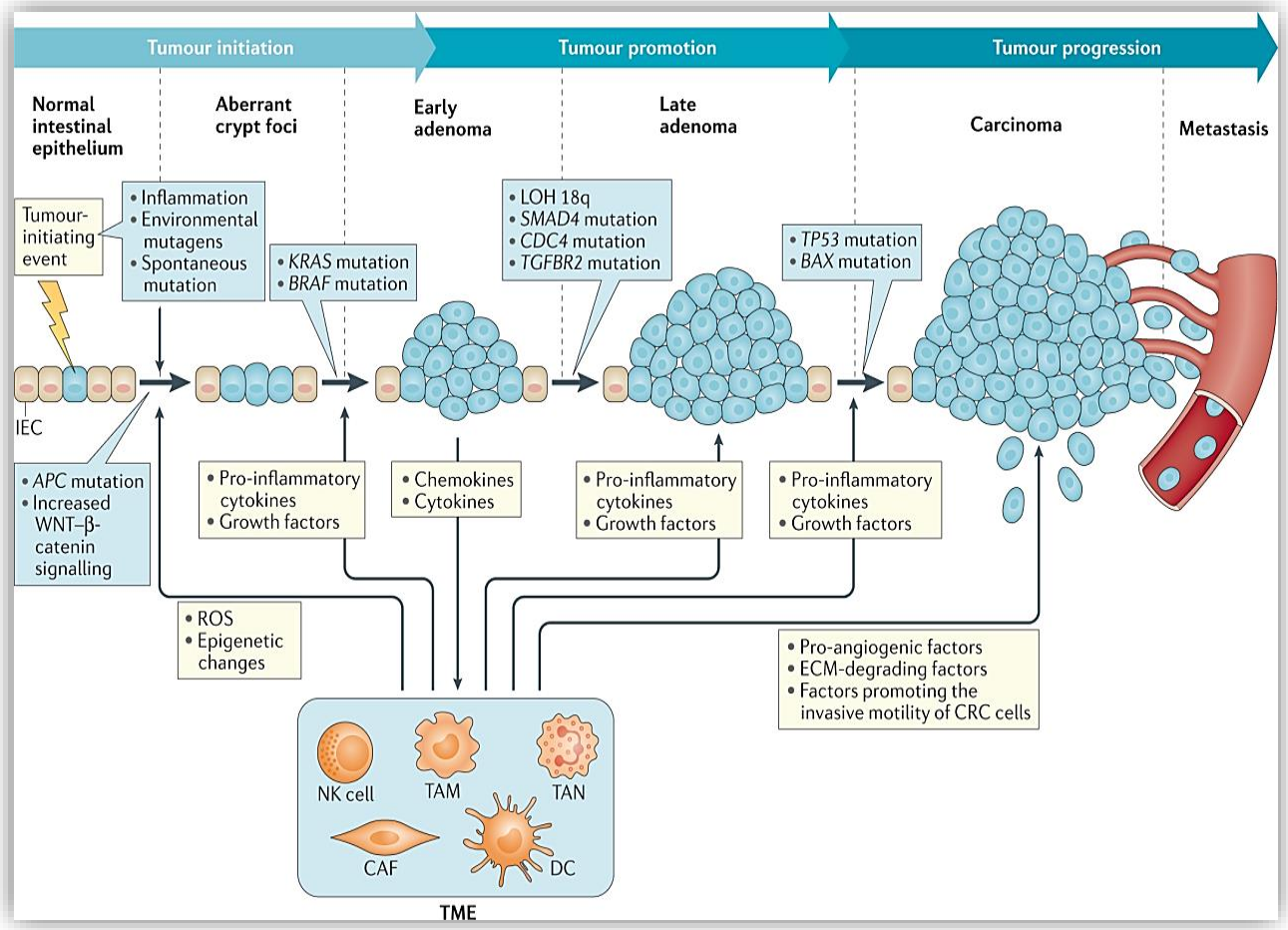

Figure 7. The figure depicts tumor initiation and promotion mechanisms in colorectal cancer **(Schmitt and Greten, 2021).**

3.3.3 The Role of the Microbiome and Mycobiome in colorectal cancer

Pathogenic bacteria and their metabolites, such as E. coli, Fusobacterium nucleatum, and Bacteroides fragilis, bacterial metabolites can also promote tumorigenesis by releasing pro-inflammatory signals such as tumor necrosis factor (TNF) and IL-17. Loss of surface barrier

function allows commensal and pathogenic bacteria from the intestinal lumen to invade, resulting in a tumor-promoting inflammatory response in myeloid cells. The following are the findings of a survey conducted by the National Institute of Standards and Technology: (NIST). Fungi detected by the immune system can create a pro-tumorigenic inflammatory environment by secreting IL-17A and IL-22. Immunity can be suppressed by the microbiota and mycobiota by decreasing pro-inflammatory cytokines like TNF and IL-6 or by recruiting immunosuppressive cells. APC stands for antigen-presenting cell, DC stands for dendritic cell, and NK stands for natural killer **(figure 8) (Schmitt and Greten, 2021).**

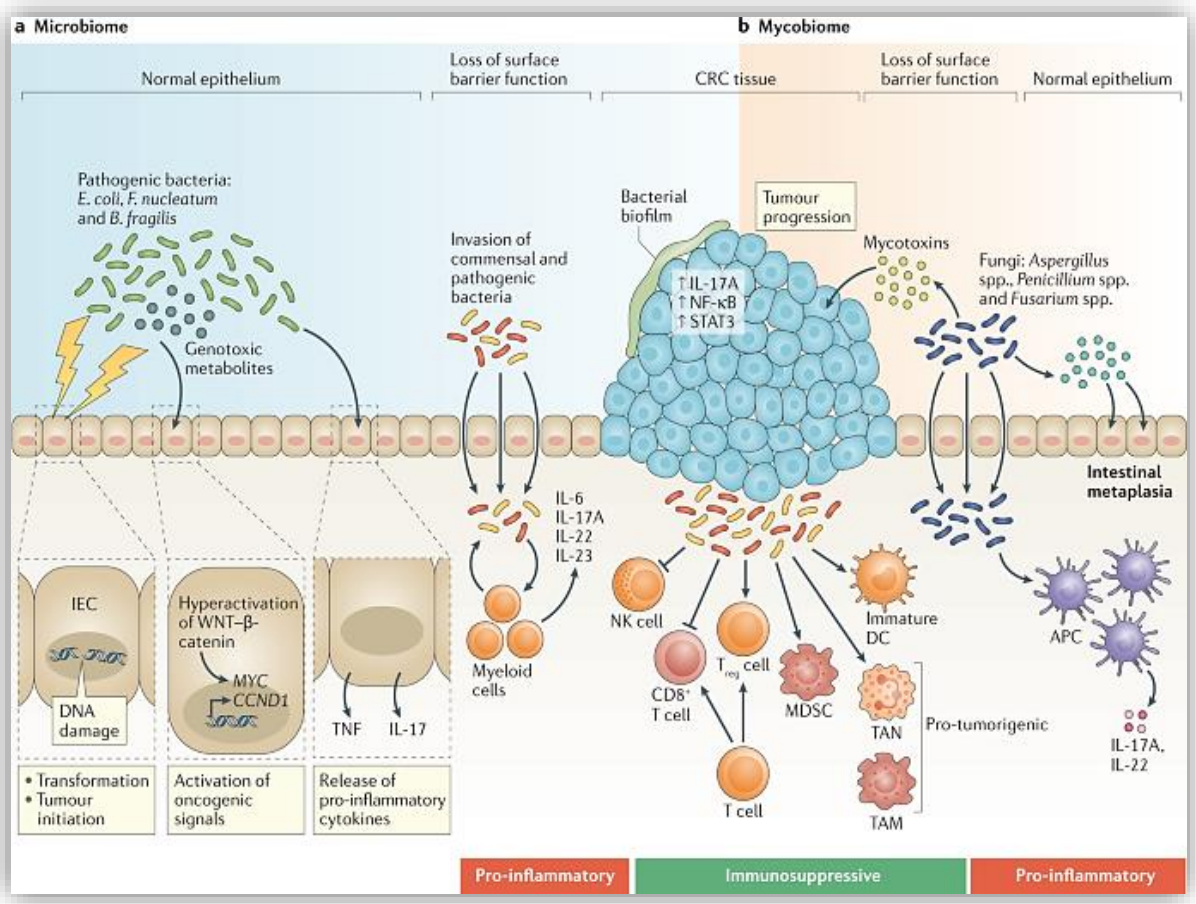

Figure 8. The figure depicts the roles of the microbiome and mycobiome in colorectal cancer. **(Schmitt and Greten, 2021).**

3.4 Epidemiology of colorectal cancer

CRC is the second most common cancer in women and the third most common cancer in men globally. In the United States, 0.16 million new CRC cases are expected in 2020, rising to 0.21 million by 2040. In 2020, Japan is expected to have 148,500 new CRC cases and 60,000 CRC deaths, with the number of incident cases expected to reach 0.16 million after two decades. Furthermore, Russia, India, Germany, Brazil, the United Kingdom, Italy, and France are among the top ten countries with the highest incidence of CRC cases in 2020. We presented estimates for CRC incident cases **(Figure.9)** and deaths **(Figure. 10)** in the top ten countries in 2020 and projections for 2040 **(Xi and Xu, 2021).**

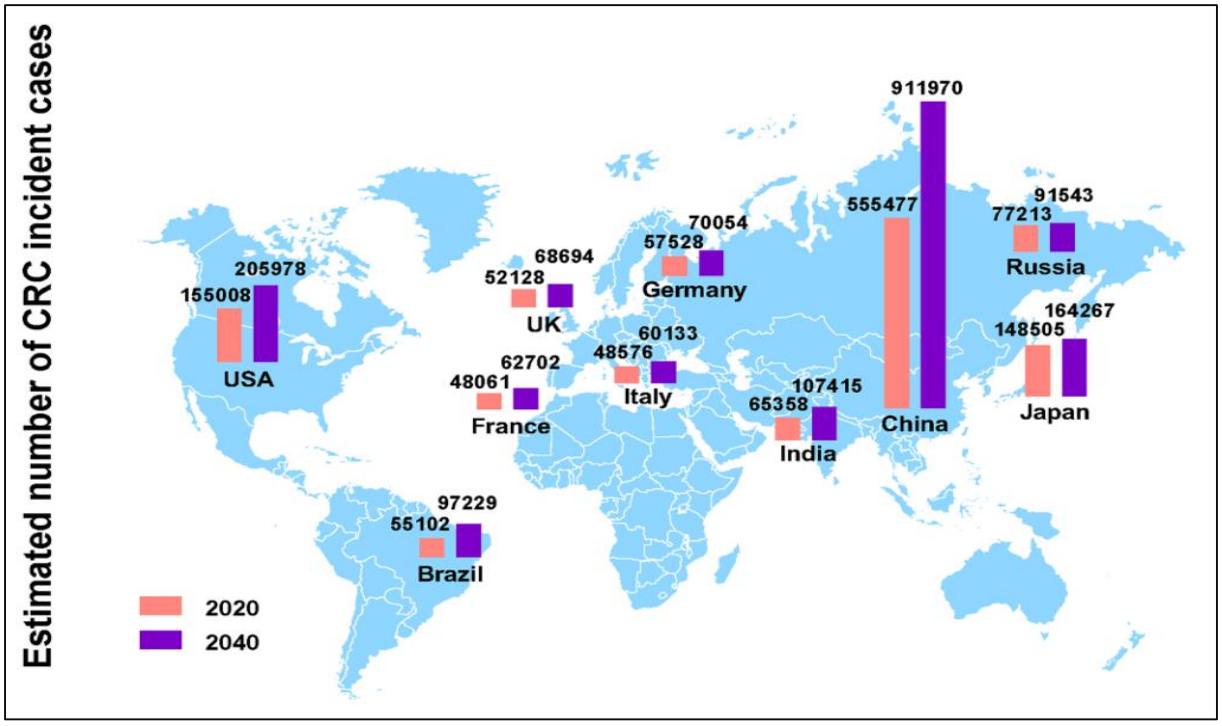

Figure 9. The number of new CRC cases in the top 10 countries with the highest incident cases in 2020 and projections for 2040 (Xi and Xu, 2021).

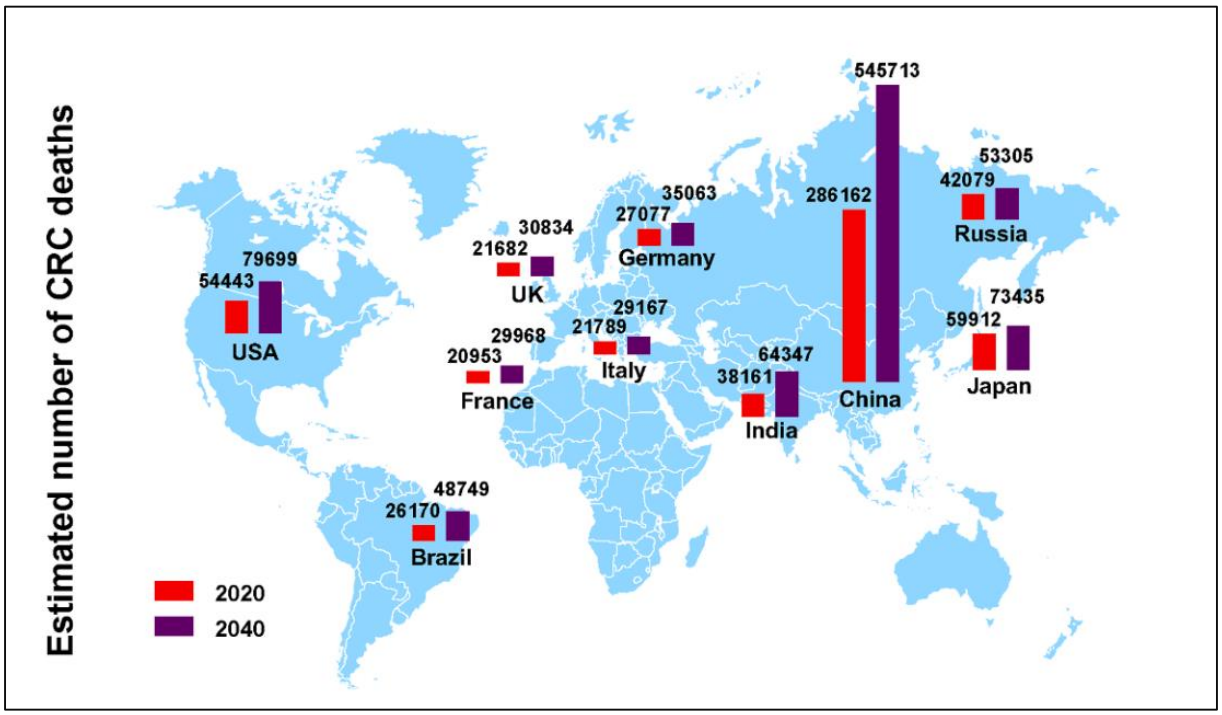

Figure 10. Deaths from CRC in the top 10 countries with the highest incident cases in 2020 and projections for 2040 (Xi and Xu, 2021)

3.4.1 Epidemiology in Africa

In Africa, CRC is the sixth most prevalent type of cancer **(Parkin et al.,2012; Katsidzira et al.,2017)** Most instances are metastatic and advanced when they are diagnosed. Hence, there are a lot of fatalities **(Chalya et al., 2015).** Figure 11's findings demonstrate that CRC occurrences have been rising over the whole continent of Africa since 2002. The highest occurrence is in Southern Africa, followed by Northern Africa **(Figures 11A, B).** Beginning with a high frequency in Southern Africa in 2002, there has been a 1.3-fold increase since then up until 2018. Other than Southern Africa, where males are 1.2 to 2 times more likely than females to develop CRC, no significant gender differences were found in other African regions **(Figure 11C) (Hamdi et al., 2021).**

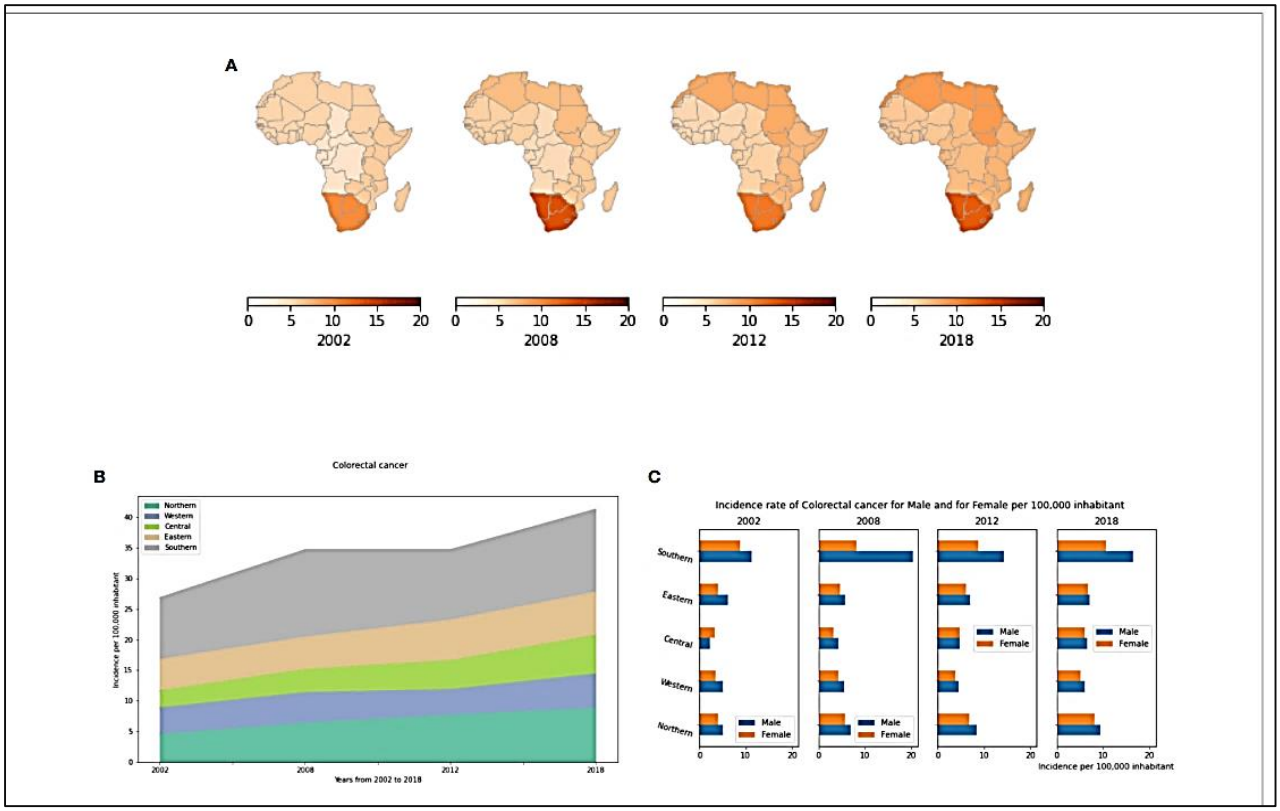

Figure 11. CRC incidence rates per year, by African region and by gender. (A) CRC incidence rates per 100,000 inhabitants in different African regions. (B) Dynamics of incidence rates from 2002 to 2018. (C) CRC Incidence Rate Gender in Africa.

3.4.2 Epidemiology in Algeria

Cancer registries have been established in Algeria **(figure 12).** They are valuable tools for researching the epidemiological characteristics of cancers. They can improve patient care because of the information gathered and the analyses performed. This tool is used by nearly 20 wilayas to collect information through a network coordinated by the Sétif register. This allowed for the evaluation of digestive cancers, which account for 25% of cancers in men and 17.5% in women. According to WHO data, CRC (9.2%) comes in second place, after lung cancer (17.8%) in men and breast cancer (25.8%) in women. According to the SAHGEED (Algerian Society of Hepato gastro-enterology and Digestive Endoscopy), Algeria is a low-risk country for CRC **(Keddad, 2019).**

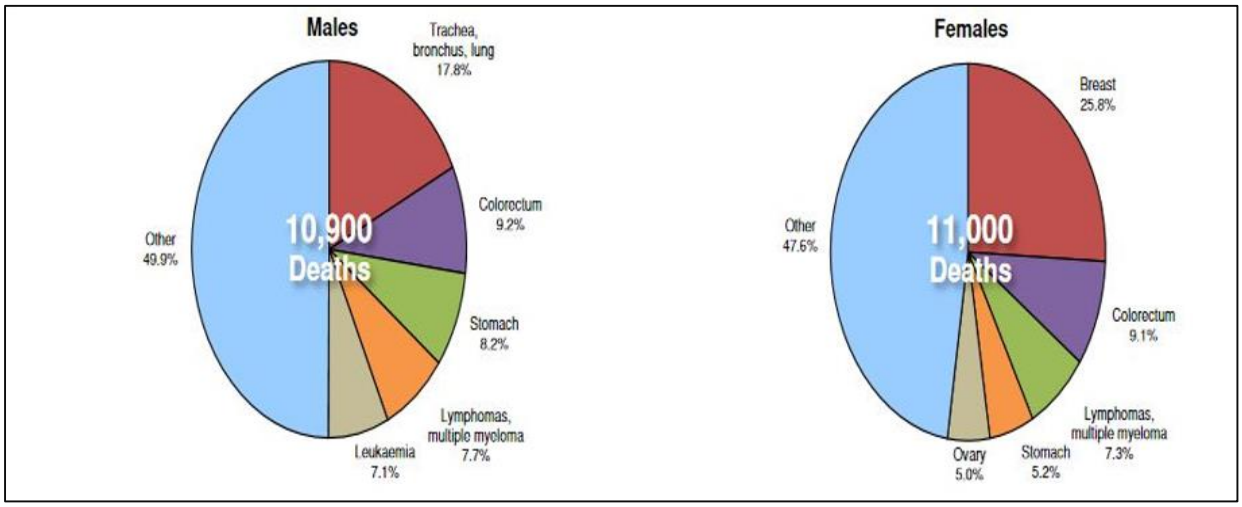

Figure 12. Cancer registries in Algeria (Keddad, 2019).

Table 1. Death rates

Total population	Total deaths
38,482,000	291,000

Table 2. Life expectancy at birth.

Male	Female
70	7

3.4.3 Epidemiological Data about the Location

The majority of tumors are situated in the rectum (37%) and sigmoid colon (31%), while their occurrence is less frequent in other regions such as the ascending colon (9%), cecum (8%), descending colon (5%), transverse colon (4%), hepatic angle (4%), and splenic angle (2%) **(Zhu C, 2015).** Approximately 65% of colon cancers occur in the region below the splenic angle, which can be easily identified through sigmoidoscopy. In contrast, 35% of colon cancers occur in the area above the sigmoid colon and cannot be detected using flexible sigmoidoscopy **(Calva AM, 2009).**

4. Screening Methods of colorectal cancer

The current methods for screening individuals who are at moderate risk and are 50 years or older involve the use of tests such as fecal occult blood test (TSOH) that have a high level of accuracy and can be performed annually using either the Guaiac or immunologic method. Another method is sigmoidoscopy every 5 years along with TSOH every 3 years, or colonoscopy every 10 years **(National Comprehensive Cancer Network Guidelines (NCCN Guidelines). Colorectal Cancer Screening. Washington: NCCN Guidelines; 2014).** The diagnostic procedures for colorectal cancer are mostly based on a patient's medical history. However, some tests like fecal occult blood tests can yield false positives due to the intake of red meat, vegetables, and fruits that contain peroxidase. Conversely, individuals who do not have a bleeding condition but consume vitamin C can also result in a false positive **(Calva AM, 2009).**

However, advancements in technology have led to the development of new techniques like PCR, which involves a specific test to identify biological genetic markers. It aims to detect mutations in specific genes that are associated with colorectal cancer. At present, the identification of colon and colorectal cancer involves the examination of concentrations of the homeobox duodenal pancreatic transcription factor (PDX-1). This factor plays a vital role in the development and proliferation of the pancreas, and its levels increase primarily in pancreatic, breast, colon, and prostate cancers as well as in metastatic tumors. In contrast, low levels are observed in primary tumors, or no levels are detected in healthy colon tissue. Therefore, PDX-1 is considered a biomarker for colorectal cancer (**Ballian N, 2008).**

5. Diagnosis of colorectal cancer

A diagnosis of colorectal cancer either results from an assessment of a patient presenting with symptoms or as a result of screening. In symptomatic patients, colonoscopy is the preferred method of investigation, but other endoscopic methods are also available or being developed. For population screening, a range of other methods can be used for primary assessment, followed by colonoscopy in case of a positive test (**Ernst J et al., 2015).**

5.1. Colorectal cancer signs and symptoms

Colorectal cancer may not show immediate symptoms, but if present, it can cause changes in bowel habits, rectal bleeding, abdominal pain, weakness, fatigue, and unintended weight loss. It can also lead to low red blood cell counts due to chronic bleeding. In some cases, the first sign may be a low red blood cell count detected through a blood test. If the cancer spreads, symptoms like an enlarged liver, jaundice, or breathing difficulties may occur. While these symptoms can be caused by other conditions, it's important to seek medical attention to determine the underlying cause

(**National Cancer Institute. Physician Data Query (PDQ). Colon Cancer Treatment. 2020. Accessed at https://www.cancer.gov/types/colorectal/patient/colorectal-treatment-pdq on February 12, 2020).**

5.2. Colonoscopy

Colonoscopy is the gold standard for the diagnosis of colorectal cancer. It has high diagnostic accuracy and can assess the location of the tumor. Importantly, the technique can enable simultaneous biopsy sampling and, hence, histological confirmation of the diagnosis and material for molecular profiling. Colonoscopy is also the only screening technique that provides both a diagnostic and therapeutic effect. Indeed, the efficacy of colonoscopy for the reduction of colorectal cancer incidence and mortality was well demonstrated (**Ernst J et al., 2015).**

5.3. Biopsy

A biopsy involves the extraction of a small tissue sample to be examined under a microscope. While other tests can indicate the presence of cancer, only a biopsy can provide a definite diagnosis of colorectal cancer. The collected sample(s) are then analyzed by a pathologist. The biopsy procedure can be conducted during a colonoscopy or surgery, and in some cases, a CT scan or ultrasound may be employed to guide a needle biopsy, which involves removing tissue from the tumor through the skin using a needle (**Libutti SK et al., 2019).**

5.4. Blood tests/ carcinoembryonic antigen (CEA).

Elevated CEA levels can suggest the spread of cancer to other body parts. However, CEA is not a definitive test for colorectal cancer, as only around 60% of individuals with colorectal cancer that has spread to other organs from the colon exhibit high CEA levels. Furthermore, other medical conditions can also cause an increase in CEA. The CEA test is primarily used to monitor colorectal cancer in individuals who are already undergoing treatment and is not suitable as a screening test (**Cancer.Net Editorial Board, 05/2022).**

Carcinoembryonic Antigen (CEA) is a glycoprotein involved in cell adhesion and serves as a tumor marker. Monitoring CEA post-operatively in CRC has been shown in multiple studies to improve overall survival. International guidelines recommend regular CEA testing every three to six months for at least three years, followed by testing every six to twelve months in the fourth and fifth years after initial surgery for localized CRC, and every two to three months in cases of metastatic CRC **(Lugat, A et al.,2021).** Carbohydrate Antigen 19-9 (CA 19-9), also known as sialyl Lewis, is a tetrasaccharide carbohydrate and a cancer antigen with higher blood concentrations in colon cancer patients, particularly those with metastatic disease **(Thomsen, M et al.,2018).** Increased amounts of CA 19-9 have been discovered in the serum of individuals with metastatic colon cancer **(Vukobrat, Z et al.,2013).**

6. Biomarkers of colorectal cancer

In colon cancer, biomarkers are detectable biological traits or chemicals that identify the presence or stage of cancer or forecast the tumor's response to treatment. Genetic, epigenetic, proteomic, or metabolic biomarkers are all possible. KRAS mutations, BRAF mutations, microsatellite instability (MSI), and DNA methylation patterns are examples of biomarkers in colon cancer **(Benson AB et al., 2018)**.

- **Common Biomarkers in CRC**

-KRAS is an oncogene KRAS encodes tiny proteins that bind to guanine triphosphate and function as a GTPase transducer. The KRAS proteins, commonly known as p21, are found on the cell membrane **(Colicelli J., 2004)**. KRAS is a biomarker commonly tested in people with advanced colorectal cancer. KRAS gene mutations have been associated with chemotherapy resistance and patients with KRAS mutations may be candidates for alternative therapies **(Van Cutsem E et al.,2009)**.

-BRAF is an oncogene that encodes the BRAF protein, also known as serine-threonine kinase, which is a MAPK pathway regulator and is associated with cell proliferation **(Chu J et al., 2022)**, acting as a prognostic biomarker and a potential therapeutic target in CRC patients **(Gong J et al., 2016)**. BRAF mutations are more common in women and people over the age of 70, are mostly detected in the right colon, and can affect any part of the colon or rectum. This mutation should be tested in stage IV patients to correctly target treatment **(Noreen F et al.,2019)**.

-Microsatellite instability (MSI) is a biomarker discovered in a fraction of colon cancers that indicates a failure in the DNA repair process. Immune checkpoint drugs, which help the immune system recognize and target cancer cells, may be more effective in tumors with a high MSI **(Le DT et al.,2017)**. MSI is found in about 15% of all colorectal cancers **(Nojadeh JN et al.,2018)**. CRCs with microsatellite instability are histopathologically characterized by mucinous poor cell differentiation, and high lymphocyte infiltration, and are most commonly found in the right colon **(DeAngelis G et al.,2018)**.

-DNA methylation abnormal methylation of tumor suppressor gene promoter regions silences these genes and promotes carcinogenesis. Researchers evaluated stool- or blood-derived DNA hypermethylation in CRC patients and controls and discovered sensitivities and specificities ranging from 53-72% to 89-100% for detecting colorectal neoplasia. Because of the genetic variability of CRC, a panel of markers is likely to be required to attain enough sensitivity for clinical relevance as a screening biomarker **(DeVos et al., 2009, Melotte V et al., 2009)**.

7. Use of Biomarkers in determining prognosis and guiding treatment decisions in colorectal cancer

A tumor biomarker test could be used in a variety of situations. These contexts of usage include risk categorization (e.g., determining germline mutations as a susceptibility marker), screening, differential diagnosis, prognosis, prediction, and monitoring. The prognosis was defined as an indication of the likelihood of an event (recurrence, distant metastases, or death) occurring in the future, regardless of the effect of prior or predicted therapy. The ability of a certain biomarker to predict the likelihood of benefit from a given therapy or class of agent (e.g., endocrine, biologic, or chemotherapy) **(Koncina, E et al.,2020)**.

The tumor's microsatellite instability (MSI) status is one example of a biomarker employed in colon cancer. MSI is a sign of poor DNA mismatch repair (MMR), a critical route for genomic stability. When compared to microsatellite stable (MSS) cancers, MSI-high (MSI-H) tumors have a higher frequency of mutations and a better prognosis and responsiveness to immunotherapy. The FDA has approved pembrolizumab, a PD-1 inhibitor, for the treatment of MSI-H colorectal cancer that has progressed after prior treatment **(André T et al.,2020).**

8. Treatment

8.1. Conventional treatment

Treatment for colorectal cancer is surgical. Chemotherapy and radiotherapy are only adjunctive treatments or sometimes only palliatives

- **Surgery:** It represents the main treatment in CRC, which consists of removing a part where cancer appears.
- **Chemotherapy:** Chemotherapy is the administration of a drug to the patient cytotoxic intended for the destruction of cancerous cells that investigations could not have detected, it can perform various functions in the CRC
  - **Adjuvant chemotherapy**: it is used in addition to surgery to remove residual cancer cells to prevent cancer recurrence or metastasis.
  - **Neo-adjuvant chemotherapy:** it aims to reduce the size of CRC before the surgery.
  - **Palliative chemotherapy aims** to increase survival and ensure patient comfort.
- **Radiotherapy:** Radiation therapy involves destroying the tumor or cancer cells using X-rays or high-energy particles. It is offered depending on the type of cancer, and its stage of the patient's general state.
  - **Curative radiotherapy:** destroy all cancer cells.
  - **Palliative radiotherapy (symptomatic):** slow down the progression of a tumor, by treating the symptoms **(Stephanie, D 2014).**

8.2. Therapeutic Targets in colorectal cancer

A medical specialist may examine the malignancy of specific cells to determine which targeted treatments will be most effective against them. Treatment of malignant growths in a particular area may include specific types **(Gupta et al., 2022).** The development of targeted therapies, particularly the targeting of the EGF receptor pathway by antibodies monoclonal anti-EGF receptors, has been a significant advancement in the management of patients with metastatic CRC (EGFR). When EGF binds to its receptor, signaling pathways are activated **(Mitry et Rachet, 2004).**

8.3. Immunotherapy in colorectal cancer

The body's disease methodologies do not always attach to specific diseases because malignant cells produce proteins that make it difficult for the resistant framework cells to recognize the disease cells as dangerous. Immunotherapy and other similar treatments work by interfering with this cycle **(Ellsworth et al., 2022).** When we talk about immunotherapy, we get to the root cause and application of tumor-infiltrating lymphocytes (TILs) in CRC immunotherapy. There is an increasing variety of investigations that support the importance of tumor immune infiltration, including lymphocytes [T cells (CD8+, Th), B cells, and natural killer (NK) cells], macrophages, dendritic cells, and neutrophils, revealing a wide patient-to-patient diversity **(Senovilla et al., 2012; Jochems and Schlom, 2011).**

CD4+ T cells play a key role in enhancing tumor control, both during effector T cell initiation and in the tumor microenvironment **(Bai et al., 2022).** Vaccines designed to induce a CD4 response have shown significant promise in improving clinical outcomes in subgroups of patients with melanoma and breast cancer **(Melssen and Slingluff CL, 2017).** While several early trials have yielded promising data, further studies are needed to verify its safety and effectiveness. Moreover, a growing number of studies have the potential to improve our understanding of NK and B cell antitumor functions, promising positive research in related fields. With insights gained from trials based on NK and B cells, novel therapeutic strategies will likely help guide clinicians toward more personalized treatment for CRC patients **(Bai et al., 2022).**

8.4. Palliative care

Palliative care experts collaborate with the individual, their family, and their PCPs to provide an additional assistance layer that complements continuing care. Palliative care can be used alongside more aggressive therapies such as medical procedures, chemotherapy, and radiation treatment. Palliative care is provided by a team of specialists, medical attendants, and other highly trained professionals **(Temel et al., 2022).** Palliative care groups are intended to improve personal well-being and satisfaction for patients and their families in addition to other forms of treatment or healing that the individual may be receiving **(Gupta et al., 2022).**

Chapter II

Anatomopathological study of colorectal cancer

1. Definition

Anatomopathology is the study of tissues and bodily fluids to detect cancerous cells, and infectious agents, and determine the cause of death **(Lewandrowski K., 2014)** It involves a variety of techniques such as microscopy and molecular testing and is interpreted by pathologists who use their knowledge to make accurate diagnoses and guide patient care (**Damjanov I et al ., 2016)** Histology, on the other hand, is a branch of biology concerned with the composition and structure of plant and animal tissues about their specialized functions. Histologists mainly examine quantities of tissue that have been removed from the living body and use techniques such as staining and electron microscopy to reveal details of tissue organization. Histochemistry is a special branch of histology that involves the chemical identification of various substances in tissues **(Britannica T., 2013).**

2. The importance of Anatomopathology in the Diagnosis and Treatment of CRC

Anatomopathology plays a critical role in the treatment of colorectal cancer by identifying abnormal or cancerous cells, determining the type and stage of cancer, and assessing the efficacy of chemotherapy or radiation therapy treatments. Pathologists can analyze biopsied tissue samples from the colon or rectum and provide information on the extent of cancer, which helps guide treatment decisions. In addition, histology techniques can help identify certain genetic mutations that can inform targeted therapies for patients with colorectal cancer. Providing accurate diagnoses and information on disease progression, anatomy pathology is an important tool in the fight against colorectal cancer **(Arnould L., 2002).**

3. Macroscopic features of CRC

Macroscopic examination generally describes the appearance of the tumor (ulcerated, perforated, well-defined, infiltrating lesion, vegetative, ulcers-infiltrative, solid, cystic, papillary, diffusely infiltrative of the linitis type, stenosing, etc...). These characteristics, which appear in an account report of anatomopathological examination, give the most often useful indications for diagnosis (benign/malignant, histological type) or allow to explain a posteriori particular symptomatology or imagery. They give much less often indications of the tumor prognosis. For example, a macroscopic papillary appearance of an extrahepatic bile duct or gallbladder tumor has been associated with a better prognosis. In the colon and rectum, and except for perforated tumors, it seems on the other hand that the appearance of the tumor does not influence the prognosis **(Arnould L., 2002).**

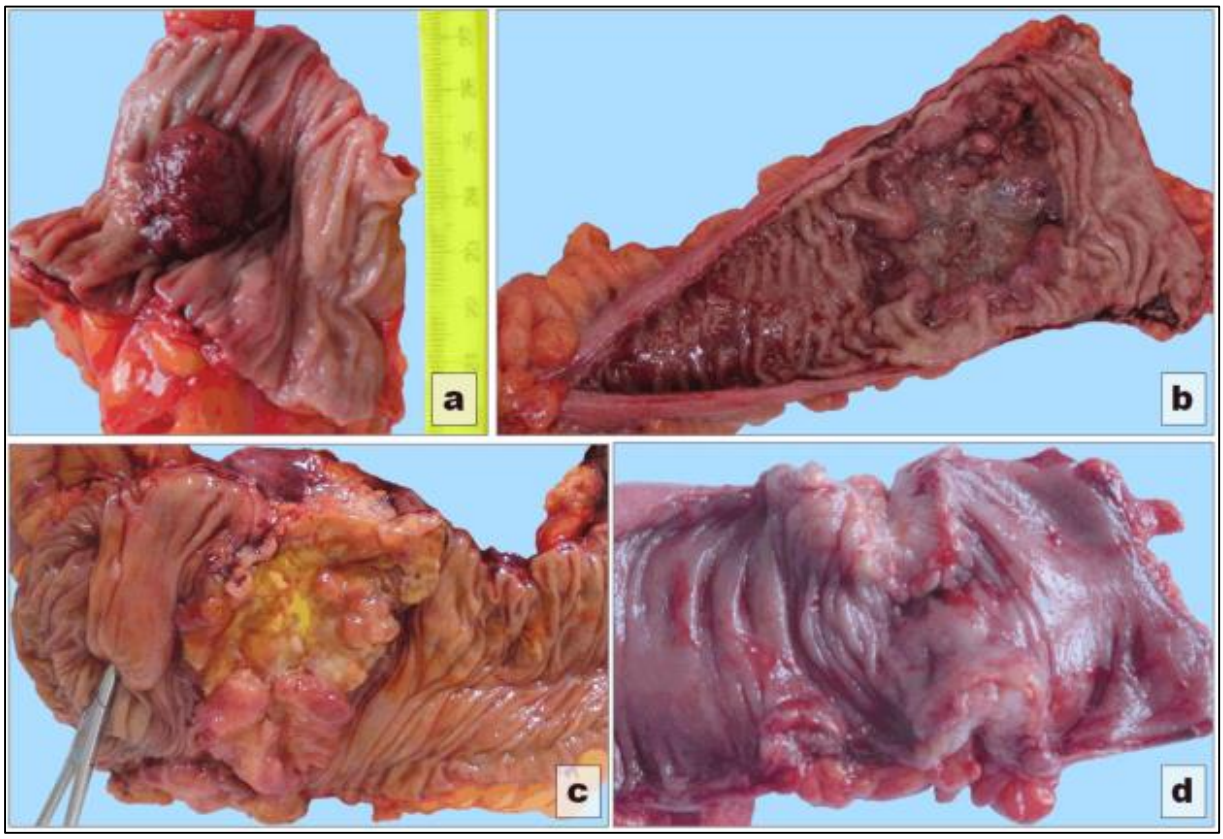

Figure 13. Types of tumor gross aspect: (a) Vegetant (V); (b) Ulcero-infiltrative (UI); (c) Vegetant and ulcerated (VU); (d) Infiltrative (I) **(Rom J Morphol Embryol, 2015).**

3.1.Vegetating or budding forms

These types of growth are frequently associated with necrosis and infection, and they are more commonly observed in the right colon. They develop inside the colon, protruding into the colonic lumen, and rarely invade surrounding tissues. They can advance to form abscesses near the colon. They often present as an outwardly growing mass within the colonic lumen, exhibiting irregular, soft, and sessile characteristics. This particular appearance is frequently observed in the right colon and is seldom associated with narrowing or obstruction **(Lamrani, 2008).**

3.2. Pure ulcerated forms

They are exceptional, it is most often a mixed lesion, ulcer-vegetative or ulcer-infiltrative **(Lamrani, 2008).**

3.3.Infiltrating forms

They are seen especially on the transverse colon and the left colon. They are infiltrating and stenosing, thickening, and stiffening the colonic wall. It is the classic tumor in "ferrule" responsible for occlusive forms **(Lamrani, 2008).** To detect the presence of a polyp in the colon, it is necessary to carry out a colonoscopy for only she can afford to see him.

4. Microscopic feature of CRC

4.1 Precursor tumors

An adenoma is a non-cancerous tumor composed of glandular epithelial cells that develop within a gland and exhibit a structure resembling the gland. In the case of colonic adenomas, they always show dysplasia, indicating localized abnormal epithelial growth **(Stevens et al., 2004).** Intestinal adenomas are polyps formed by glandular tissue protruding from the intestinal mucosa. While adenomas are generally benign, they are considered precancerous and can potentially progress into malignant structures. Hyperplastic polyps, on the other hand, have no malignant potential **(Mărginean CO et al., 2016).** Adenomas are further categorized as villous, tubular, or tubulovillous, depending on their characteristics. Villous adenomas have over 75% villous features on the surface, such as finger-like projections, while tubular adenomas consist mostly of tubular glands and have less than 25% villous features **(Myers DJ et Arora K., 2010).** Although villous adenomas are more prone to malignancy due to their larger surface area, when considering the overall surface area, all types of adenomas have an equal chance of becoming malignant **(Bujanda L et al., 2010).**

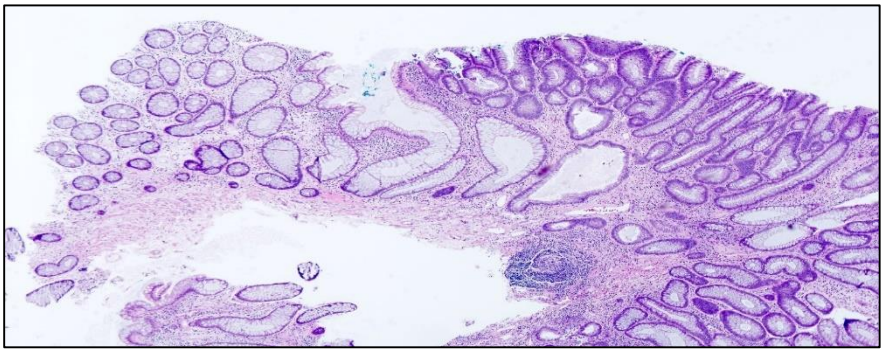

Figure 14. Microscopic (histologic) images of Tubular adenomas **(Andrew L et al., 2021).**

- Adenomas are classified according to their:
    1. **Endoscopic appearance:** sessile, pedunculated, flat.
    2. **Degree of dysplasia:** low grade, high grade, depending on cytonuclear abnormalities and architecture.
    3. **Microscopic (histological) architecture:** tubular, tubule villous, villous. The term invasive adenocarcinoma is reserved for colonic adenocarcinomas, lesions extending beyond the muscular mucosa **(Stevens et al., 2004).**

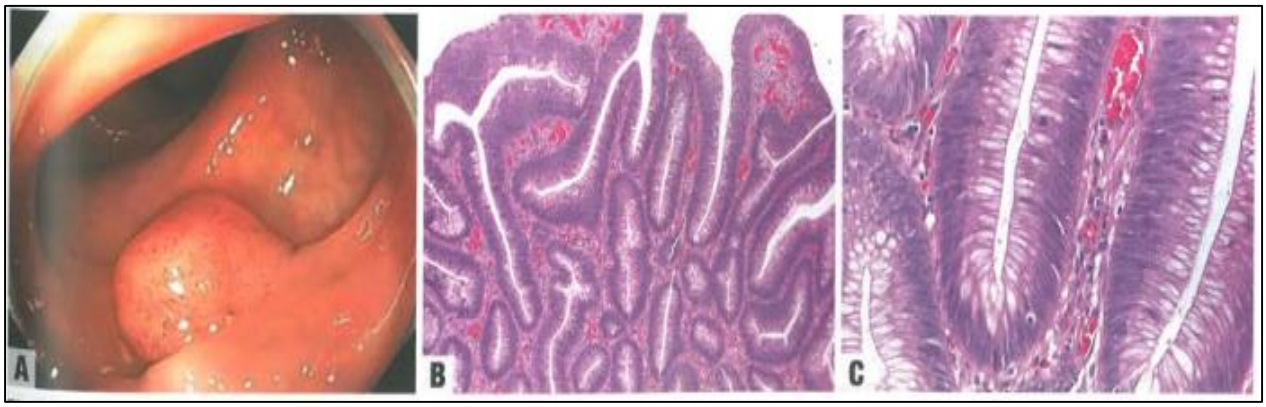

Figure 15. Colonic tubular adenoma. A) colonoscopic image: the surface of the polyp has avoided orifices; B) low-power image of variably shaped tubules without complex architecture, composed of cells with low dysplasia with only mild or moderate nuclear enlargement and pleomorphism; C) high-power image of tubules lined by cells with mild or moderate nuclear enlargement and pleomorphism **(WHO Classification of Tumors Editorial Board, 2019).**

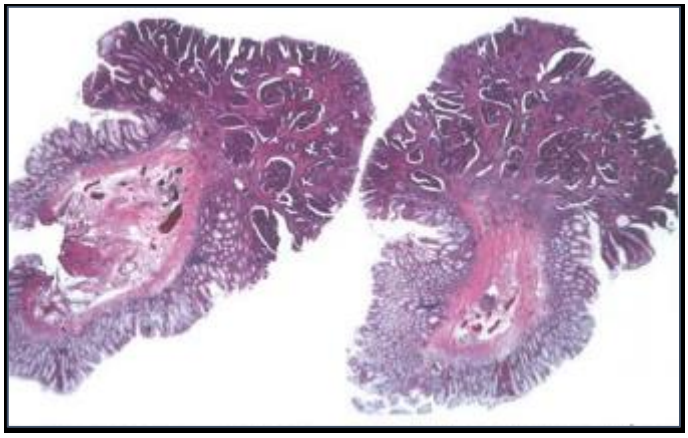

Figure 16. Tubulovillous adenoma with invasive carcinoma. An ultra-low power image of an example with high-grade dysplasia shows invasion into the smooth muscle in the head/neck region of the polyp by small clusters and single adenocarcinoma cells **(WHO Classification of Tumors Editorial Board, 2019).**

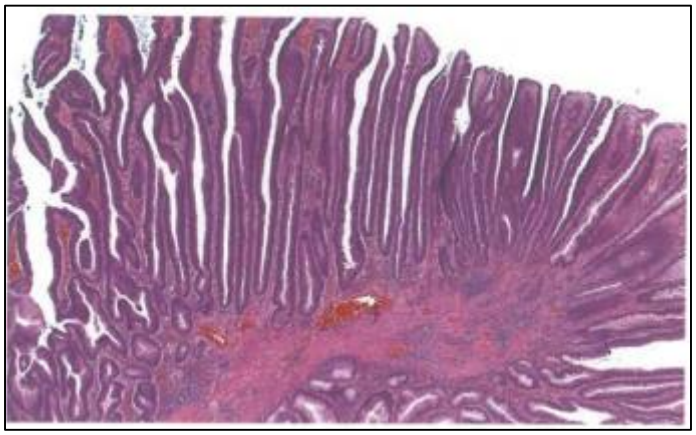

Figure 17. An area of villous architecture within Adenoma **(WHO Classification of Tumors Editorial Board, 2019).**

4.2 Malignant epithelial tumors

There are various histopathologic types of colorectal carcinoma, including adenocarcinoma not otherwise specified (NOS), mucinous adenocarcinoma, poorly cohesive carcinoma, signet ring cell carcinoma, medullary adenocarcinoma, adenosquamous carcinoma, undifferentiated carcinoma and neuroendocrine carcinoma (comprising small cell carcinoma and large cell neuroendocrine carcinoma) **(American Joint Committee on Cancer • 2017).** Most colorectal cancers are adenocarcinomas (95%). The other histological forms are rarer **(Lasser, 1994).**

a. Iieberkühnian adenocarcinomas

They are developed at the expense of the glandular epithelium whose cytology and architecture they tend to closely or remotely reproduce **(Lasser, 1994).**

- Depending on their degree of mucus secretion and the organizational characteristics of the tumor cells, adenocarcinomas are well differentiated, moderately, differentiated, and poorly differentiated. As differentiation decreases, the frequency of lymph node metastases increases and survival decreases.
- Depending on the secretory capacity of adenocarcinomas, a distinction is made between mucinous or colloid adenocarcinomas (secreting a lot of mucins) and non-mucinous adenocarcinomas. ADK Lieberkühnien is more or less differentiated **(Viguier et al., 2003)**.

Table 3. Histologic grade (G) **(American Joint Committee on Cancer, 2017).**

G	G definition
GX	Grade cannot be assessed
G1	Well-differentiated
G2	Moderately-differentiated
G3	Poorly-differentiated
G4	Undifferentiated

- **Well-differentiated ADK (70–75%):** This type of ADK has a glandular structure with regular tubes, which is bordered by a coating formed of cylindrical cells with a nucleus that is uniform in size and shape, the cell polarity is evident, and the glandular epithelium stays unistratified. Mucosecretion can be increased or decreased. On stroma reaction, the quantity of vascular fibro balanced with tumor proliferation.
- **Moderately differentiated ADK (10%):** has somewhat irregular glandular tubes rich in mitoses, solid cell masses hollowed down with cribriform cavities, and un evident or missing cell polarity.
- **Little or undifferentiated ADK (5%):** is distinguished by extremely infrequent, irregular glandular tubes embedded in an extensive fibrous inflammatory stroma drenched in single cells or aggregated in clusters or strips of undifferentiated cells. Periodic acid shift stains indicate mucus secretion, which is quite moneme.

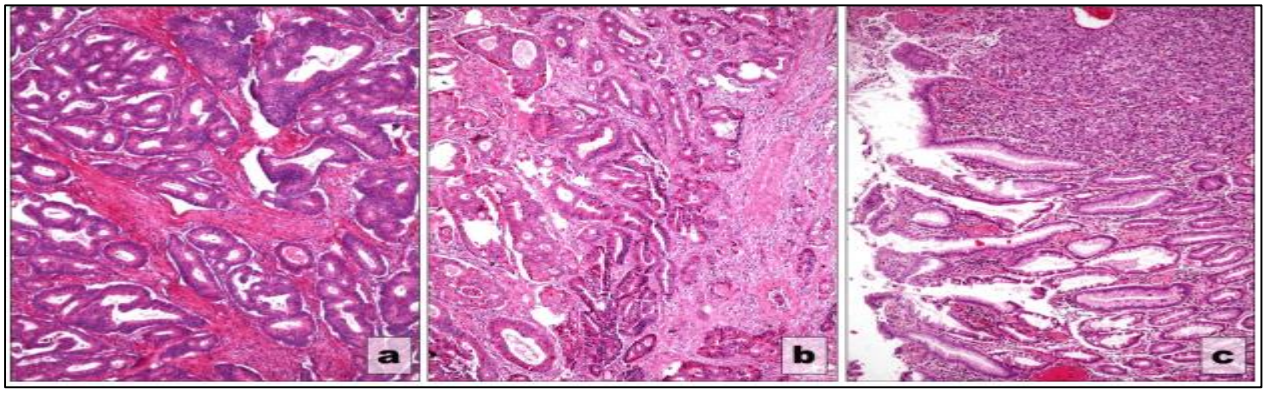

Figure 18. Tumor grading: (a)Well-differentiated adenocarcinoma; (b) Moderately differentiated adenocarcinoma; (c) Poorly differentiated adenocarcinoma **(Rom J Morphol Embryol, 2015).**

b. Mucinous ADK (mucous colloid)

These colloid or mucinous ADKs account for 17% of tumors and are distinguished by vast regions of mucus speckled with independent tumor cells, with a gelatinous colloid macroscopic appearance. Tumor cells develop either tube-distended glandular more or less regularly ruptured in enormous areas of mucus either clusters or spans histologically **(Mallem, 2010).**

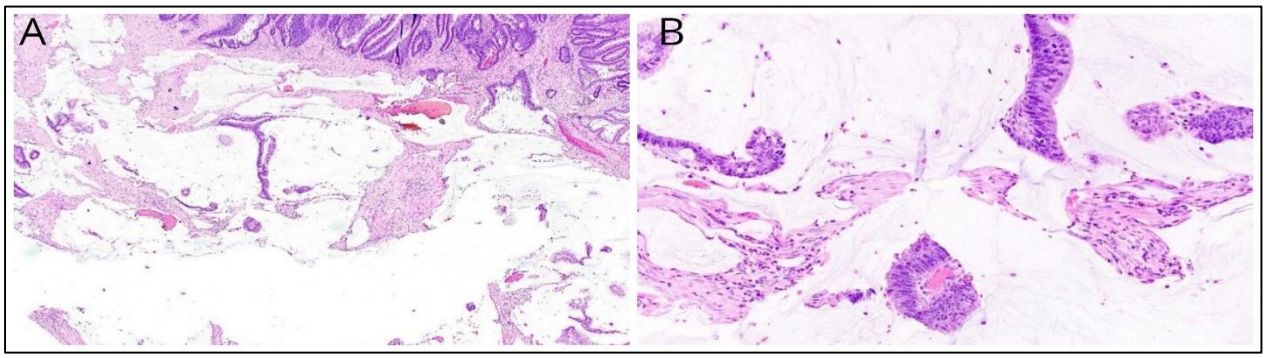

Figure 19. Microscopic (histologic) images of Mucinous adenocarcinomas **(Raul S et Gonzalez, M.,2021).**

c. Adenosquamous carcinoma

Adenosquamous carcinoma is an uncommon colorectal tumor that has both adenocarcinoma and squamous cell carcinoma. Only a few examples have been mentioned in the literature (**Toumi, O et al.,2018).** ADKs with a high concentration of Malpighian foci. They are most likely caused by polyps undergoing squamous metaplasia. They're fantastic. Furthermore, the prognosis is worse than ADK's current form (**Mallem, 2010).**

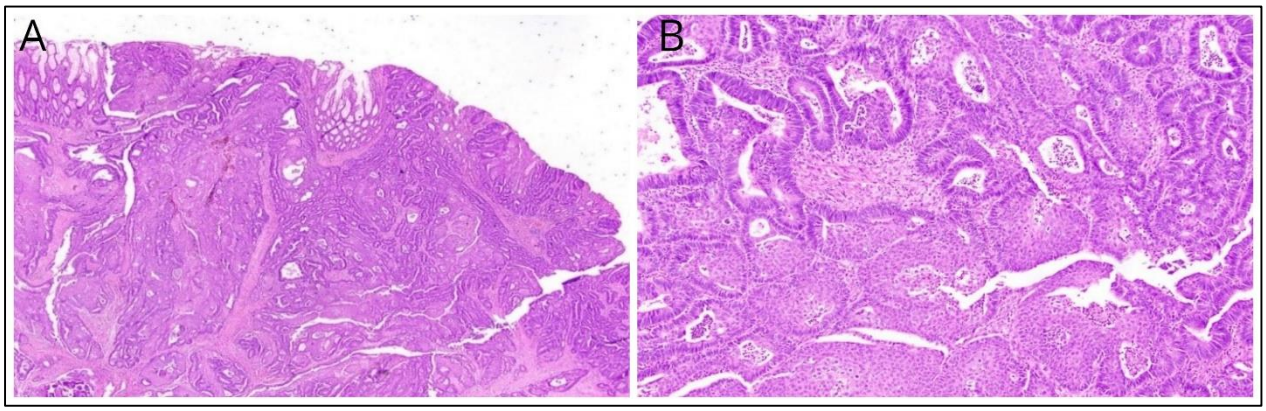

Figure 20. Microscopic (histologic) images of Adenosquamous carcinoma **(Raul S et Gonzalez, M.,2021).**

d. Signet Ring cell carcinoma

This variant is distinguished by the presence of more than 50% mucus with intracellular localization, giving the appearance of a bezel ring. They are uncommon, accounting for approximately 2 to 4% of all tumors **(Stevens et al, 2002)**. Ring cell carcinoma kittens are colloid carcinomas with intracellular mucus. It indicates the growth of separate cells with vacuolar cytoplasm and nuclei pushed to the periphery **(Zeitoun et al., 2014; Camilo et Thomas, 2016)**.

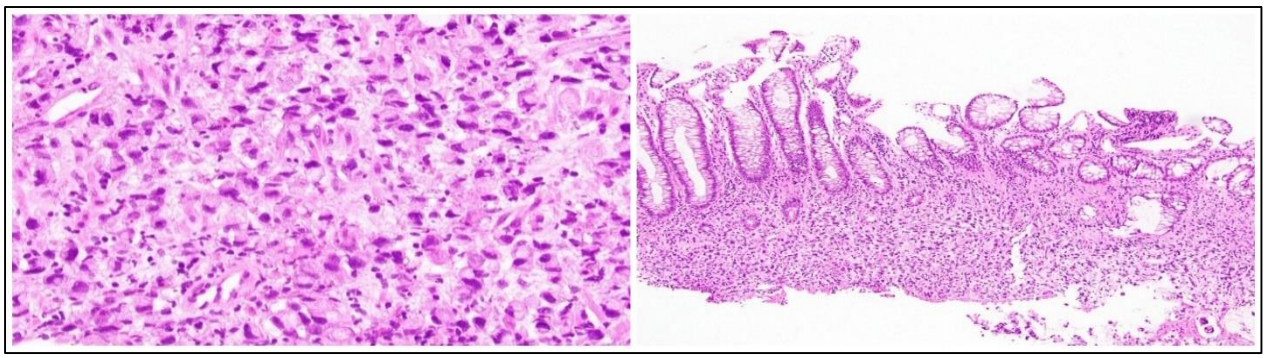

Figure 21. Microscopic (histologic) images of Signet ring cell carcinoma **(Raul S et Gonzalez, M.,2021).**

5. Classification of colorectal cancer

The TNM system aids in determining the disease's anatomical scope, and the sum of the three elements can be used to determine the tumor's overall stage. With tumors graded from I through IV, with stage IV being the most severe stage, this technique allows for simplification. Carcinoma in situ, which is not now considered cancer but could develop into it in the future, is referred to as stage 0 in this context-**(Leslie SW et al.,2023)**.

5.1 Clinical classification

Table 4. Definition of Primary Tumor (T) **(American Joint Committee on Cancer, 2017).**

T Category	T criteria
Tx	Primary tumors cannot be assessed
T0	No evidence of a primary tumor
Tis	Carcinoma in situ, intramucosal carcinoma (involvement of lamina propria with no extension through muscularis mucosae)
T1	Tumor invades the submucosa (through the muscularis mucosa but not into the muscularis propria)
T2	Tumor invades the muscularis propria
T3	Tumor invades through the muscularis propria into peri colorectal tissues
T4	Tumor invades the visceral peritoneum or invades or adheres to adjacent organ or structure
T4a	Tumor invades through the visceral peritoneum (including gross perforation of the bowel through the tumor and continuous invasion of the tumor through areas of inflammation to the surface of the visceral peritoneum)
T4b	Tumor directly invades or adheres to adjacent organs or structures

Table 5. Definition of Regional Lymph Node (N) **(American Joint Committee on Cancer, 2017).**

N category	N criteria
Nx	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	One to three regional lymph nodes are positive (tumor in lymph nodes measuring ≥0.2mm), or any number of tumor deposits are present and all identifiable lymph nodes are negative
N1a	One regional lymph node is positive
N1b	Two or three regional lymph nodes are positive
N1c	No regional lymph nodes are positive, but there are tumor deposits in the • subserosa • mesentery • or non-peritonealized pericolic, or perirectal/ mesorectal tissues
N2	Four or more regional nodes are positive
N2a	Four to six regional lymph nodes are positive
N2b	Seven or more regional lymph nodes are positive

Table 6. Definition of Distant Metastasis (M) **(American Joint Committee on Cancer, 2017).**

M category	**M criteria**
M0	No distant metastasis by imaging, etc.; no evidence of tumor in distant sites or organs (This category is not assigned by pathologists.)
M1	Metastasis to one or more distant sites or organs or peritoneal metastasis is identified
M1a	Metastasis to one site or organ is identified without peritoneal metastasis
M1b	Metastasis to two or more sites or organs is identified without peritoneal metastasis
M1c	Metastasis to the peritoneal surface is identified alone or with other site or organ metastases

5.2 Classification of pathological TNM

The T and N categories are represented by the pT and pN categories.

At least 12 lymph nodes should be examined histologically during a regional lymphadenectomy.

- **PN0:** If lymph nodes are not affected but the minimum number is not reached, classify them as pN0.
- **pM1** indicates a histologically confirmed metastasis. **(Brierley et al. 2017)**.

5.3 Stage Groups

Table 7. Colorectal cancer tumor-node-metastasis staging **(American Joint Committee on Cancer, 2017).**

When T is...	**And N is…**	**And M is…**	**Then the stage group is…**
Tis	N0	M0	0
T1, T2	N0	M0	I
T3	N0	M0	IIA
T4a	N0	M0	IIB
T4b	N0	M0	IIC
T1_T2	N1/N1c	M0	IIIA
T1	N2a	M0	IIIA
T3_T4a	N1/N1c	M0	IIIB
T2_T3	N2a	M0	IIIB
T1_T2	N2b	M0	IIIB
T4a	N2a	M0	IIIC
T3_T4a	N2b	M0	IIIC
T4b	N1_N2	M0	IIIC
Any T	Any N	M1a	IVA
Any T	Any N	M1b	IVB
Any T	Any N	M1c	IVC

6. Correlation between the staging and grading prognosis of CRC

The assessment of staging and grading plays a crucial role in determining the outlook for patients diagnosed with colon cancer. The widely employed American Joint Committee on Cancer (AJCC) staging method for colon cancer is utilized extensively and categorizes tumors based on their level of invasion, involvement of lymph nodes, and the presence of distant metastases. Conversely, the tumor grade reflects the extent of cellular differentiation and significantly predicts the outcome. As the grade of the tumor increases, the prognosis worsens. High-grade tumors exhibit aggressive behavior and demonstrate a poor response to treatment. Precise staging and grading are vital in guiding treatment decisions and forecasting the prognosis of individuals with colon cancer (**DeVita VT et al., 2015)**

Experimental Part

Materials and Methods

I. The retrospective study

I.1. Population study and framework

A retrospective study was conducted on CRCs in the Department of Pathological Anatomy and Cytology of the Hospital University Center Ibn Badis Constantine, during a period of 3 years (from 2020 to 2022). Based on the admission data from the hospital records and all anatomopathological reports, 60 patients (23 females and 37 males) with colorectal cancer were included in this study, with an age range from 27 to 87 years. Compiling data from medical records allowed us to establish the inclusion and exclusion criteria.

- **Patient recruitment (inclusion)**

The inclusion criteria comprise the cancer type and location to comprehensively analyze the population. The study includes patients with primary colon and/or rectal cancer and those presenting with both colonic and rectal cancer.

- **Patient exclusion**

Patients with colorectal metastasis of another cancer were excluded from this study.

II. Anatomopathological study

The specimens obtained from colorectal resection were substantial samples obtained by surgery, measuring several tens of centimeters. These samples were then examined macroscopically. The macroscopic examination plays a critical role in managing these samples by enabling targeted sampling of the lesions, ensuring an accurate diagnosis, and a thorough evaluation of the cancer's progression. This examination involves determining the extent of colon wall invasion by cancer (infiltration degree) and identifying potential spread to nearby lymph nodes. All samples, including operative specimens and biopsies, were sent to the pathology laboratory for microscopic analysis following the sampling process. This analysis, known as an anatomopathological examination or histopathological examination, is the only definitive method to ascertain whether the sampled lesions are cancerous. It provides essential histological evidence. This subsequent examination aims to examine the entire tumor and the collected lymph nodes, allowing for a more precise assessment of the extent of the cancer.

1. Tissues samples

All tissue specimens obtained either through biopsy or surgical resection were sent to the pathology laboratory after colonoscopy or surgery. The specimens arrive with a digestive information sheet that includes details such as the patient's name, gender, age, and location of the lesion. The operative specimen arrives from the operating room fixed in 10% diluted formalin. The purpose of this fixation is to preserve the structures and immobilize the antigens in situ, preventing damage to the structures and preserving the antigens from being washed away by subsequent reactive baths. The samples were then examined in the macroscopy room, where the pathologist washed, measured, weighed, dissected, and macroscopically described.

1.1 Samples preparation

- **Step 01: Macroscopic study**

The sampler must label the containers containing the biological sample at the time of collection to prevent any errors regarding the individual's identity. The label should include the patient's name, first name, date of birth, and the date. Macroscopy is a visual diagnosis where the doctor places a suspicious sample directly into a previously labeled cassette. This step is performed in the macroscopy room **(Figure 22),** where all received specimens are prepared under the fume hood.

Figure 22. Macroscopy room.

- Materials for macroscopy :

Figure 23. Macroscopy material.

- **In the event of an operating part or organ**

During the process of handling an operating part or organ, several organized steps are followed. Firstly, the operative specimen is cleansed using running water. Precise measurements of the specimen are then taken, including its length and circumference. The size of the tumor is assessed, and its visual characteristics are described. Additionally, the appearance of the colonic mucosa surrounding the tumor is evaluated, noting the presence or absence of additional lesions such as polyps. A macroscopic description of the tumor is provided, including its shape, whether budding, ulcerating, or infiltrating, with specific features recorded if present.

Tissue fragments are extracted from both the tumor mass and the surgical resection boundaries. The number of lymph nodes is identified and documented, and the cassettes are labeled with the corresponding specimen number. The fragments, sliced into thin sections measuring 2 to 3 mm by 1 to 2 cm, are then placed into the cassettes and preserved in a 10% formalin solution (HCHO) for 24 hours to ensure optimal specimen fixation. It is important to note that these sections are obtained from the tumor's area of greatest infiltration within the colon wall, as well as from both sides of the tumor and the surgical resection margins. The key macroscopic steps involved in a colectomy specimen are summarized in **(Figure 24)** and **(Figure 25).**

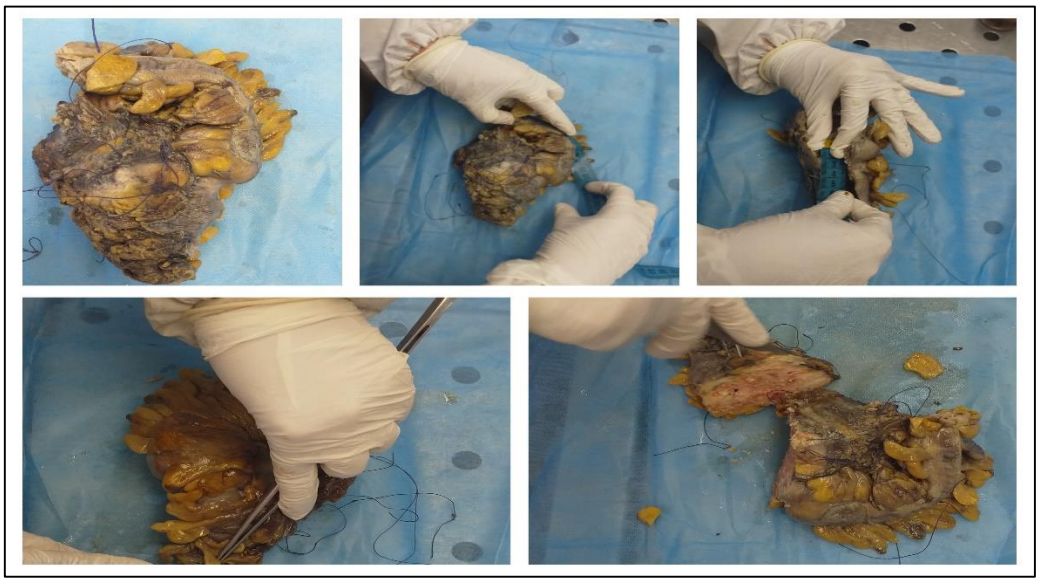

Figure 24. Colectomy specimen; measurement and cut.

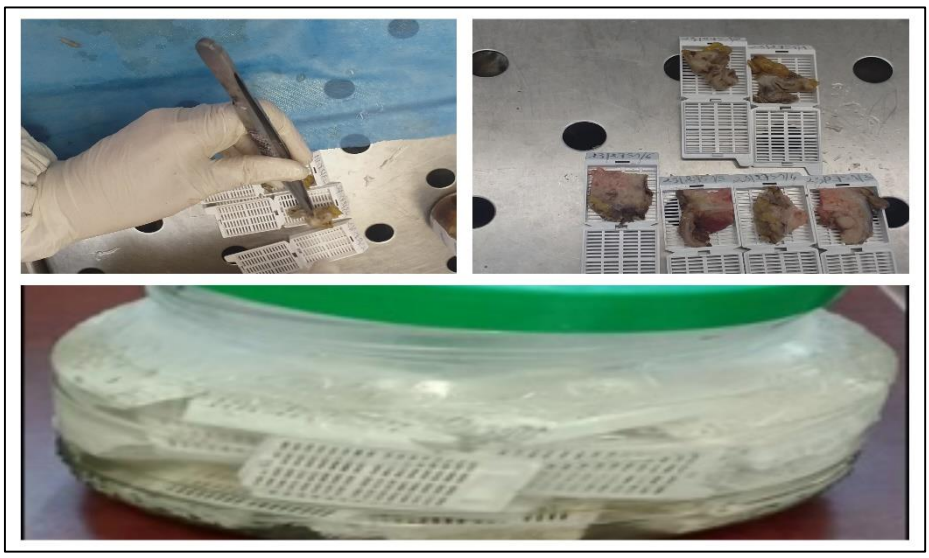

Figure 25. Fragments were placed into cassettes and then preserved in a formalin solution.

- **In the case of a Biopsy**

The gathered samples are directly placed in cassettes without the requirement for a macroscopic examination, and they are preserved in formalin.

➢ **Step 2: Tissue processing**

The removal and replacement of intra and extracellular water in tissues with paraffin is a crucial step in the technique. This process is automated using a tissue processing apparatus called a technical, equipped with 12 trays. The cassettes containing the tissue samples in vials are placed

inside the technical for a duration of 20 hours as shown in (Figure 5). The technical performs three consecutive steps: dehydration, alcohol removal and clearing, and paraffin embedding. During the dehydration phase, the vials containing the cassettes move through the 12 trays in a specific sequence. This includes seven trays of ethyl alcohol with increasing concentrations ranging from 70% to 100% (1 hour and 30 minutes for each tray) to achieve gentle dehydration and prevent cell shrinkage.

Next, the specimens pass through three trays of xylene (1 hour 30 minutes for each tray) to remove any remaining alcohol (de-alcoholization) and clarify the specimens. Finally, the samples are placed in two heated trays of paraffin for a duration of 2 hours to complete the impregnation stage.

Figure 26. Dehydration.

- **Step 3: Inclusion**

Embedding involves the introduction of a homogeneous, solidifiable, and chemically neutral substance into the tissue under study, typically paraffin, which is widely used for this purpose. The main goal of embedding is to facilitate the production of thin and uniform sections as depicted in (Figure 6). This process is carried out using a specialized apparatus and involves the following steps: firstly, the cassettes containing the tissue samples are placed on the heated compartment of the apparatus, which is set at a temperature of approximately 75°C to remove the paraffin.

Next, the samples are extracted from the cassettes using forceps. Then, the samples are positioned and securely placed in metal molds. The upper part of the cassette, which contains the specimen number, is used to cover the samples, and they are allowed to cool on the apparatus in the cold compartment at a temperature of approximately -65°C. Finally, the blocks containing the embedded samples are transferred to a freezer where they solidify and become ready for sectioning.

Figure 27. Paraffin embedding (Inclusion).

- **Step 4: Sectioning**

The microtome is used to obtain tissue slices from the paraffin blocks. To begin the cutting process, the blocks are securely placed in the microtome. Excess paraffin is removed, and the cutting typically starts at a thickness of 25µm. The microtome is then adjusted to a thickness of 3µm to obtain thin tissue sections. After cutting, the sections are placed on a heating plate to facilitate spreading. Subsequently, the sections are transferred onto slides and placed in a slide holder. To complete the dehydration process, the slide holder with the slides is placed in an oven at a temperature of 56°C **(Figure 28).**

Figure 28. Sectioning.

- **Step 5: Sides Staining**

Staining is a critical step in the histopathological technique, enabling the differentiation of the fundamental components of the cell, such as nuclei and cytoplasm. Hematoxylin-eosin (HE) staining as shown in **(Figure 29)** is commonly used for this purpose, and it involves several organized steps. Initially, the slide holder containing the slides is placed in xylene for 30 minutes to remove any remaining paraffin. Subsequently, the slide holder is transferred to ethanol and kept for 18 minutes. The slides are then rinsed with distilled water for 2 minutes to ensure proper hydration.

Next, the slide holder is placed in hematoxylin for 10 minutes to stain the nuclei. Afterward, the slides are once again rinsed with distilled water for 2 minutes. To provide contrast, the slide holder is then moved to Eosin for 3 minutes. Following this, the slides undergo another 2-minute rinse with distilled water. To complete the staining process, the slide holder is placed in ethanol for 10 minutes for dehydration. Finally, the slide holder is transferred to xylene for 30 minutes to clear the slides before further analysis.

Figure 29. Slides Staining.

- **Step 6: Mounting**

Mounting the stained section between a slide and cover slip is essential for microscopic examination. The glass coverslip, secured with resin, serves multiple purposes. It ensures high transparency and refractive index, provides mechanical protection to the specimen, and helps maintain the vibrancy of the stain for an extended period **(Figure 30).**

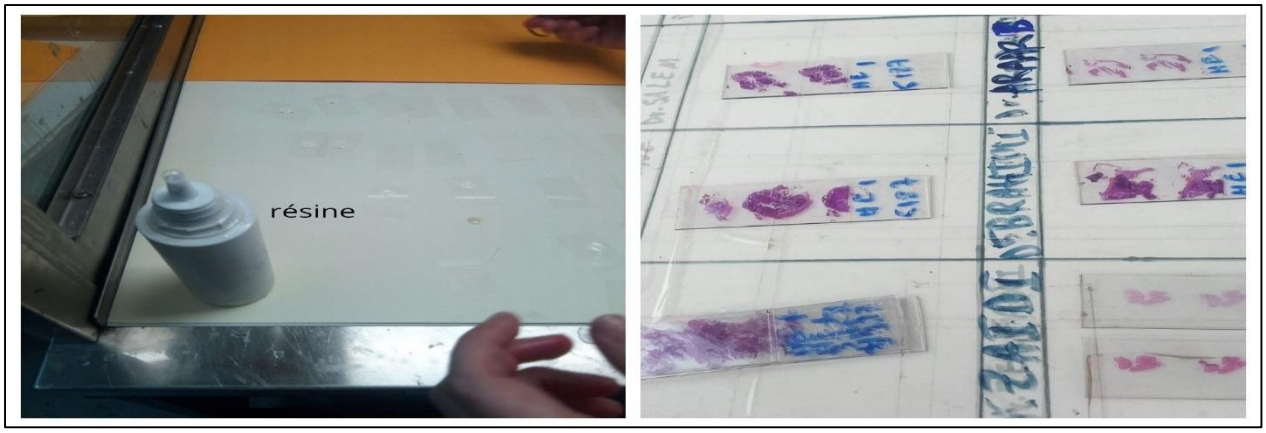

Figure 30. Mounting.

- **Step 7: Microscopic study**

The slides were examined usually using a computer-connected optical microscope, allowing for the visualization and recording of the observed images. Initially, the examination was conducted at low magnification using specifically flat objectives to obtain a comprehensive overview of the tumor. Subsequently, higher magnification was employed to analyze cellular and nuclear details more closely. This examination plays a crucial role in generating a detailed descriptive report, accurately documenting the stage and grade of the disease **(Figure 31).**

Figure 31. visualization of the slides under an optical microscope.

III. Immunohistochemistry technique (IHC)

This step takes place after the anatomopathology examination. Its purpose is to diagnose and determine the appropriate therapy. Thus, a new section is made from the previous blocks, but unlike the previous section, it involves retrieving the film slides from a water bath using special slides: silanized slides. The protocol for slide preparation involves a series of steps **(Figure 32).**

Firstly, the slide holder is placed in xylene for 15 minutes to remove paraffin (deparaffinization). The slides are then immersed in ethanol for 15 minutes for fixation. Next, an antigen retrieval solution is prepared in a water bath at 98°C. The slides are rinsed with distilled water for 10 minutes before being placed in the antigen retrieval solution for 40

minutes in the water bath, revealing antigens masked by antagonist molecules. After removal from the water bath, the slides are allowed to cool for 10 minutes. They are then dipped in TBS1 solution for 5 minutes, followed by a dip in TBS2 solution for another 5 minutes. Each tissue section is circled with Dako-Pen to limit reagent diffusion. A humid environment is prepared, and the slides are covered with a tray for incubation in the dark. Afterward, a peroxidase inhibitor H2O2 is added and incubated for 30 minutes in the dark. The slides are washed with distilled water for 5 minutes and rinsed in TBS solution for an additional 5 minutes.

The primary antibody is added and incubated for 30 minutes in the dark. Following this, the slide holder is placed in TBS1 for 5 minutes, then in TBS2 for another 5 minutes. The secondary antibody is added and incubated for 30 minutes in the dark. The slide holder is returned to TBS1 and rinsed in TBS2 for 5 minutes. Subsequently, 20µl of DAB is added and incubated for 10 minutes in the dark. The slides are then rinsed with distilled water and counterstained with hematoxylin for microscope examination. Finally, the slides are observed and interpreted under an optical microscope.

Figure 32. The different steps of immunohistochemistry.

Results and discussion

Results

1. The epidemiological study results

a) The Gender

Out of 60 patients diagnosed with CRC in our study, 37 cases were men, with a percentage of 62%, whereas 23 cases were women, representing a percentage of 38% **(Figure 33), (Table 8).**

Table 8. The distribution of patients with colorectal cancer by Gender.

Gender	Number	Percentage (%)
Men	37	62
Women	23	38
Total	60	100

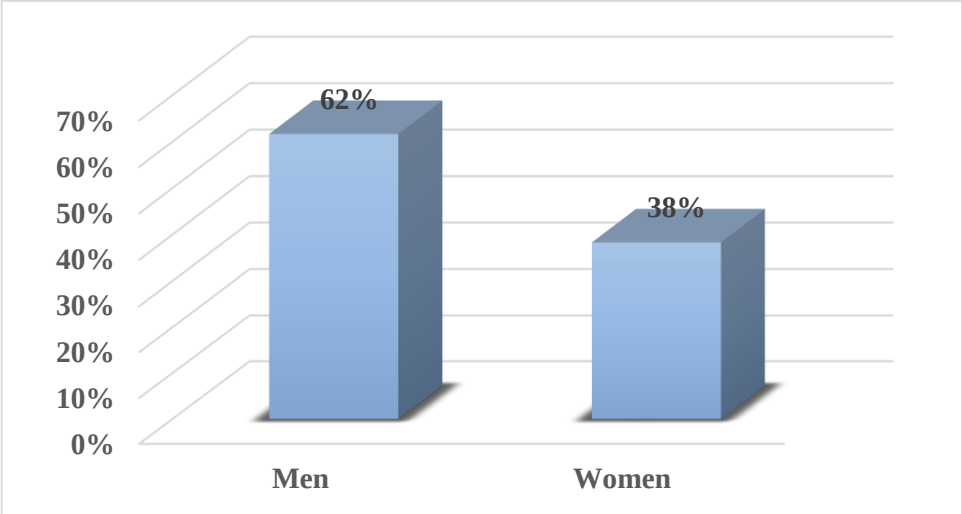

Figure 33. The distribution of patients with colorectal cancer by Gender.

b) Age range

In our study, 5 different age ranges were indicated for the study population (60 patients). 31 patients aged from 60 to 80 years, accounting for approximately half of the study population (52%), while 32% was recorded in the next range. 40 to 60 with 19 patients diagnosed positive. However, low rates were equally recorded for both 20 to 40 years and those who are beyond 80 years old with a percentage of 8% of the total recorded patients. Notably, no cases under the age of 20 were documented in this population **(Figure 34), (Table 9).**

Table 9. The distribution of patients with colorectal cancer by Age.

Age	Number	Percentage (%)
< of 20 year	0	0
[20-40[	5	8
[40-60[	19	32
[60-80[	31	52
> of 80 year	5	8
Total	60	100

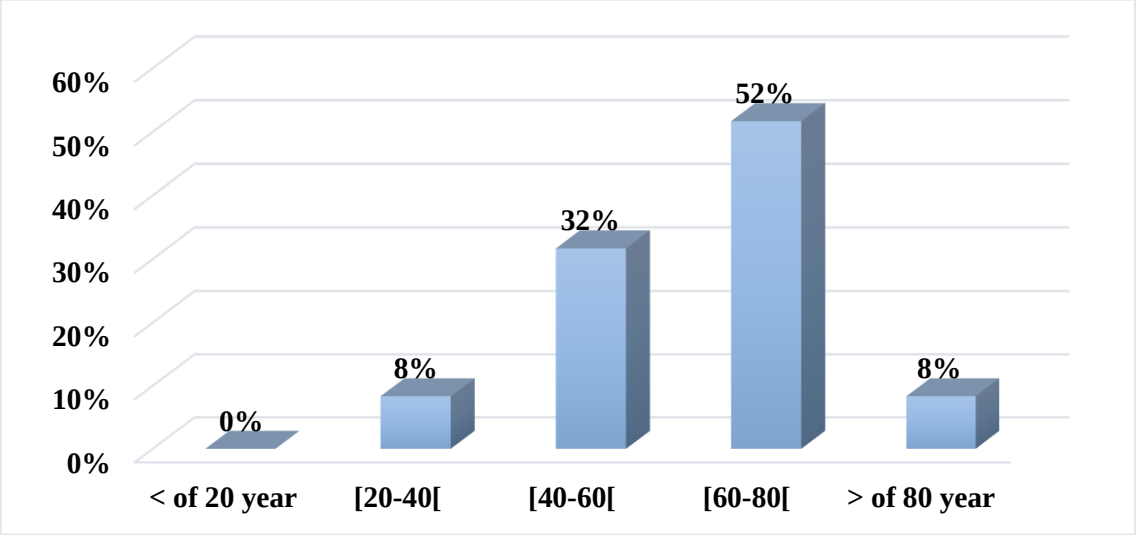

Figure 34. The distribution of colorectal cancer by Age.

c) Tumor location

In the 60 diagnosed colorectal cancer (CRC) patients, the samples were taken from different locations in the colon. A total of 17 samples were obtained from the rectum, which for 28% of the total samples, whereas 11 samples were taken from the sigmoid colon, representing 18% of the patients. Additionally, 12% of the samples, were collected from the ascending colon (7 patients). Only 3 samples were obtained from the descending colon, comprising 5% of samples, while a total of 22 samples were collected as unspecified colon sections, representing 37% of the studied cases. **(Figure 35), (Table 10).**

Table 10. The distribution of patients with colorectal cancer by tumor location.

Location	Number	Percentage (%)
Unspecified colon	22	37
Rectum	17	28
Sigmoid colon	11	18
Ascending colon	7	12
Descending colon	3	5
Total	60	100

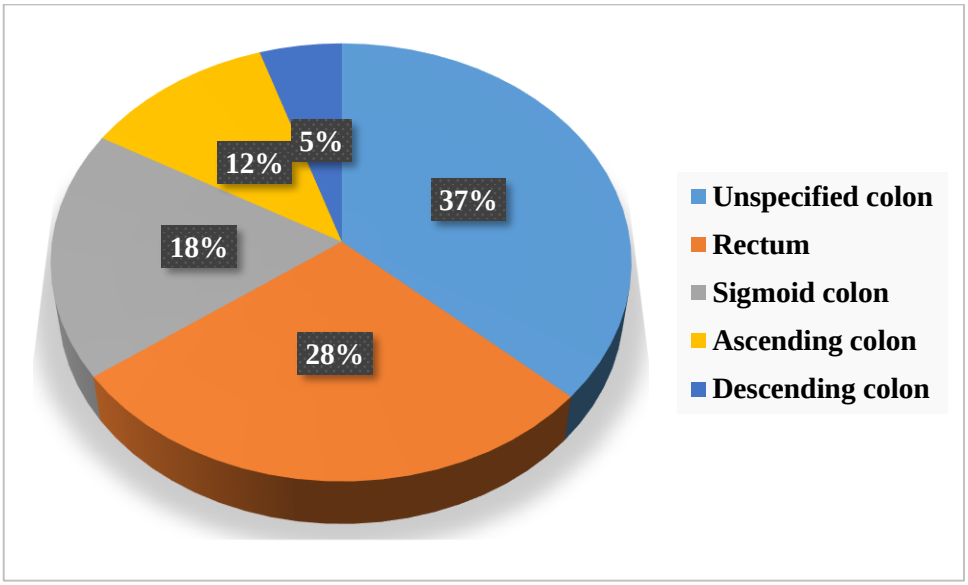

Figure 35. The distribution of colorectal cancer by tumor location

d) Tumor type

The 60 samples from CRC patients were also diagnosed and classified on a histopathological basis. The majority of cases (42 in total) were identified as well-differentiated adenocarcinoma (ADK), accounting for 70% of the samples, while only 3 samples were found to be poorly differentiated ADK, representing 5% of the cases. 15 samples were identified as moderately differentiated ADK, which represents 25% of the samples. **(Figure 36), (Table 11).**

Table 11. The distribution of adenocarcinomas according to the degree of differentiation.

degree of differentiation.	Number	Percentage (%)
Well-differentiated ADK	42	70
moderately differentiated ADK	15	25
poorly differentiated ADK	3	5
Total	60	100

ADK: adenocarcinoma

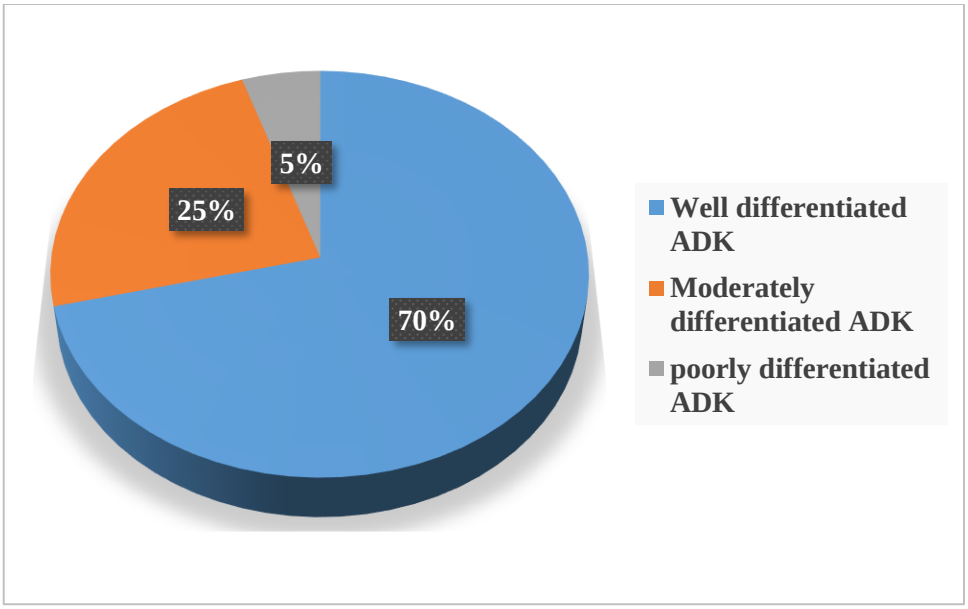

Figure 36. The distribution of adenocarcinomas according to the degree of differentiation.

e) The primary tumor T

T3 tumors were identified in 48 of the 57 patients individuals with illnesses diagnosed based on the main tumor (T), representing 84% of total tumors. Only three patients were identified with T4 tumors, reflecting 5% of the total samples. T2 tumors were found in 2 patients, accounting for 4% of the sample. Moreover, 4 patients were diagnosed with T1 tumors, representing a percentage of 7%. **(Figure 37), (Table 12).**

Table 12. The distribution of colorectal cancer (CRC) cases according to the primary tumor (T).

The primary tumor	Number	Percentage (%)
T0	0	0
T1	4	7
T2	2	4
T3	48	84
T4	3	5
Tx	0	0
Total	57	100

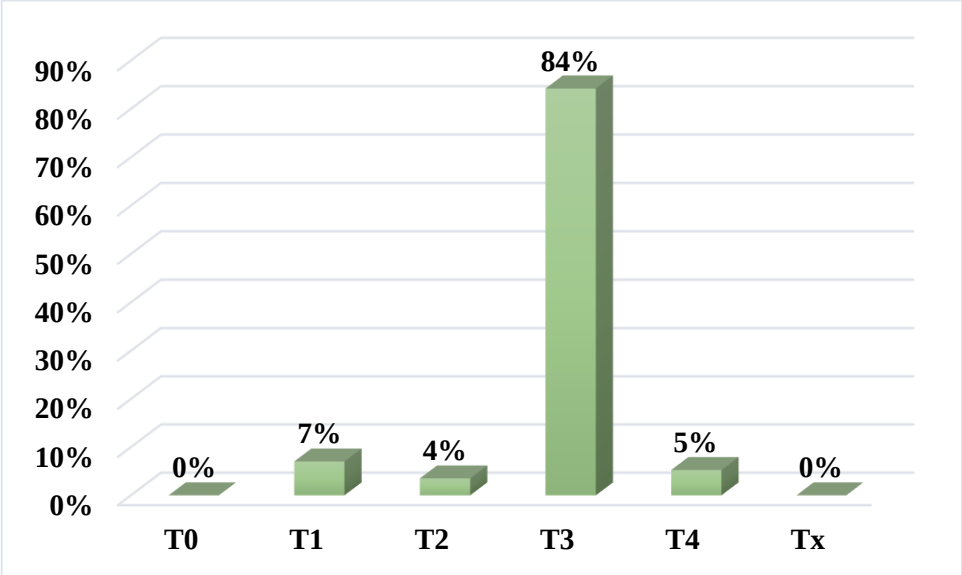

Figure 37. The distribution of colorectal cancer (CRC) cases according to the primary tumor (T).

f) The regional lymph node N

28 patients were identified with N0 status among the 57 patients diagnosed based on the regional lymph node (N), presenting a percentage of 49% of the total samples. N1 involvement was found in 9 cases, reflecting a percentage of 16%. Parallelly, 6 patients (11%) of the cases, presented an N2 involvement status, whereas only 1 patient had N3 involvement, representing a percentage of 1.75%; and 13 patients (23% of the total) had an unknown regional lymph node status (Nx) **(Figure 38), (Table 13).**

Table 13. The distribution of colorectal cancer (CRC) cases according to regional lymph node (N).

Lymph node	Number	Percentage (%)
N0	28	49
N1	9	16
N2	6	11
N3	1	1,75
Nx	13	23
Total	57	100

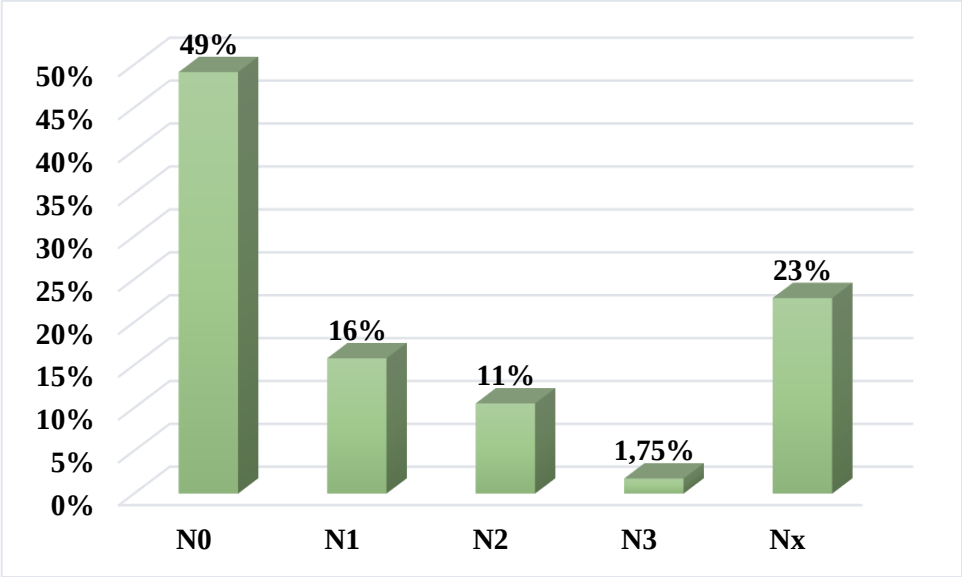

Figure 38. The distribution of colorectal cancer (CRC) cases according to regional lymph node (N).

g) Distant metastasis M

The 57 patients were diagnosed based on distant metastasis (M). Only one patient was discovered to have M0 status, representing a 1.75% prevalence. M1 metastasis occurred in two patients, accounting for a 4%percentage, while the majority (54 patients), had an unknown distant metastatic status (Mx), yielding a 95% percentage **(Figure 39), (Table 14).**

Table 14. The distribution of colorectal cancer (CRC) cases according to distant metastasis (M).

Distant metastasis	Number	Percentage (%)
M0	1	1,75
M1	2	4
Mx	54	95
Total	57	100

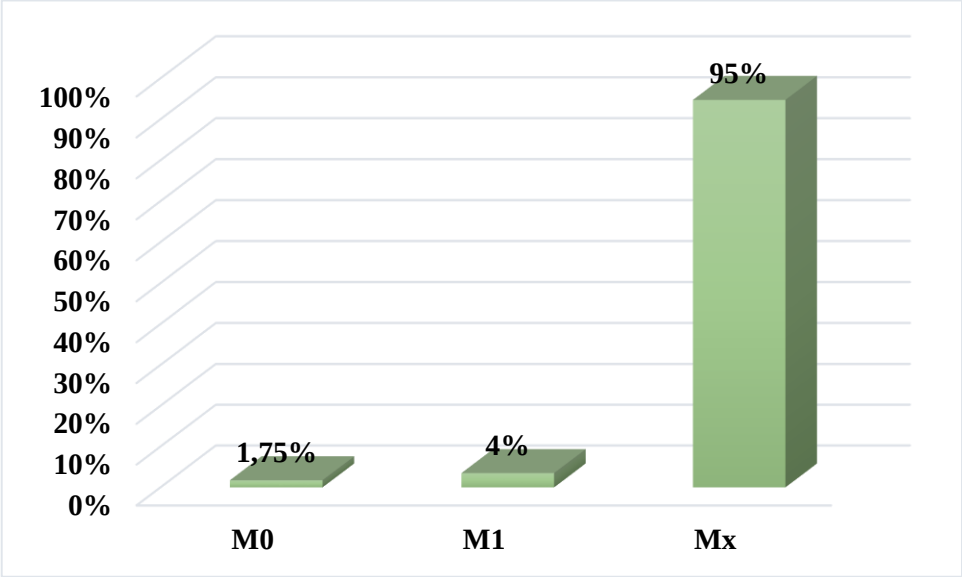

Figure 39. The distribution of colorectal cancer (CRC) cases according to distant metastasis (M).

2. Results of Anatomopathological Study

In our study, we have chosen to present the macroscopic and microscopic results of two cases of CRC. A 52-year-old male patient (1) was diagnosed with colonic cancer. And a 56-year-old female patient (2).

-**Nature of specimen (Patient 1)**: Segmental bowel resection with Colo-colonic anastomosis and drainage.

- **Nature of specimen (Patient 2)**: descending colon with the upper rectum, ileal loop total hysterectomy with bilateral annexectomy.

2.1 Macroscopy

A. Patient N°1

A colonic resection specimen of 21 cm with the distal end closed by a suture **(Figure 40).**

Figure 40. On the left: a colonic resection specimen; On the right: upon opening, there is the presence of an ulcerative and infiltrating tumor.

- ✓ Upon opening, we noted an ulcerated and budding tumor formation with stenosis, measuring 4 × 3.5 cm in circumference. It is located 2 cm from the distal end and 4 cm from the proximal end.
- ✓ Invasive tumor infiltrating the mesocolon.

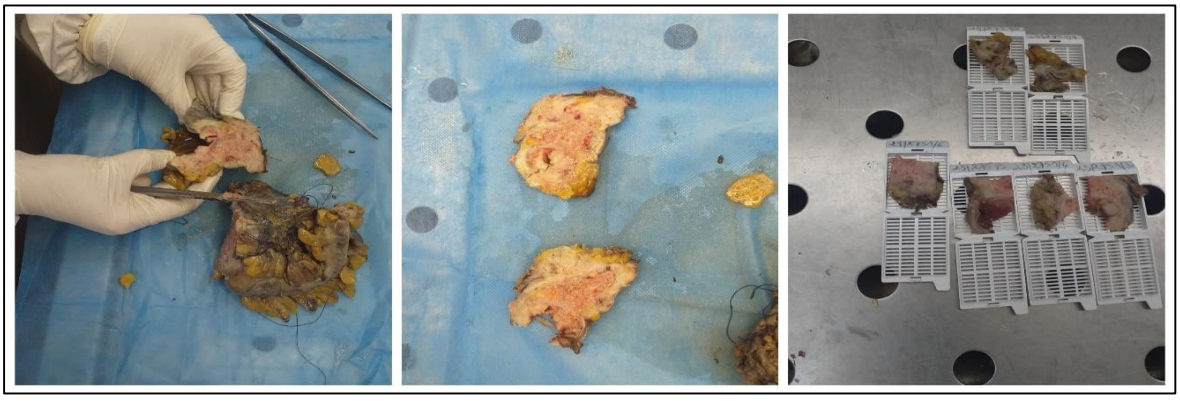

Figure 41. Taking several sections of the tumor to include the maximal depth of invasion.

- ✓ In this case, lymph node dissection yielded 14 lymph nodes.
- ✓ The resection margins must be cut and placed in separate cassettes.

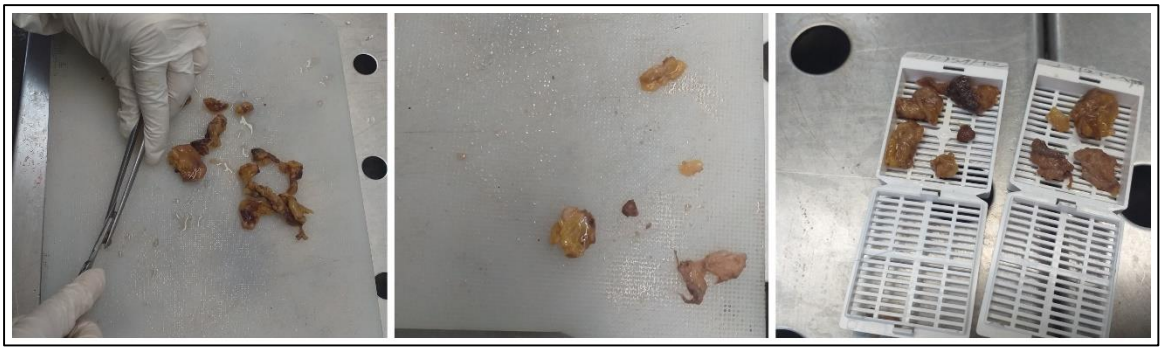

Figure 42. Mesocolonic lymph node dissection and placing the found lymph nodes in cassettes.

B. Patient N°2

Colectomy of 30 cm in length attached to a total hysterectomy with bilateral adnexectomy, uterus measuring 4/2cm, right fallopian tube measuring 3cm, and right ovary measuring 2/1.5cm **(Figure 43).**

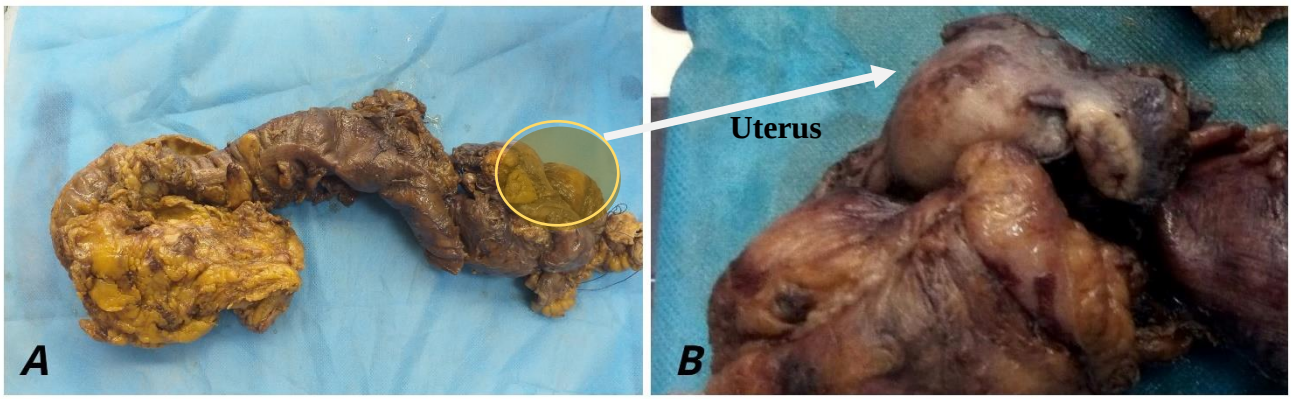

Figure 43. Left colectomy with a total hysterectomy.

- ✓ We noted the presence in the mesentery of the upper part of a poorly defined nodular formation in contact with the colonic wall, measuring 5.5/3 cm, with a fleshy whitish appearance.
- ✓ Upon opening the colon, a tumor formation measuring 5/3cm is observed. It appeared to be budding, stenosing, located 4cm from the anterior end, adherent to the uterus, and completely infiltrating the left ovary and the fallopian tube. The uterine lumen is unobstructed, and the uterine wall measures 1cm **(Figure 44).**

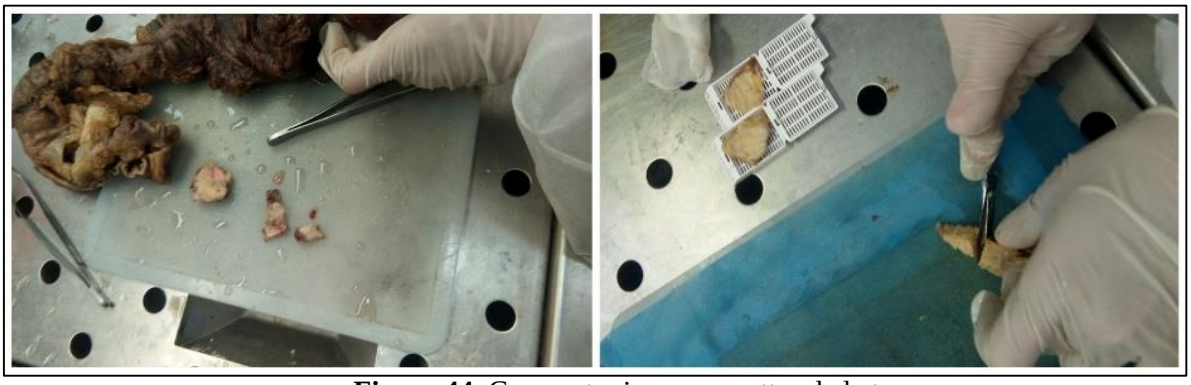

Figure 44. Coupe et mise en cassettes de la tumeur.

2.2 Microscopy

A. Patient N°1

-Classified as **T3 N0 Mx** based on the TNM staging system, it is a **moderately differentiated adenocarcinoma (ADK)**. A tumor infiltrates the serosa, displaying a glandular often cribriform architecture filled with necrotic. No vascular emboli are observed. A total of 14 lymph nodes were examined. Moreover, the margins were normal.

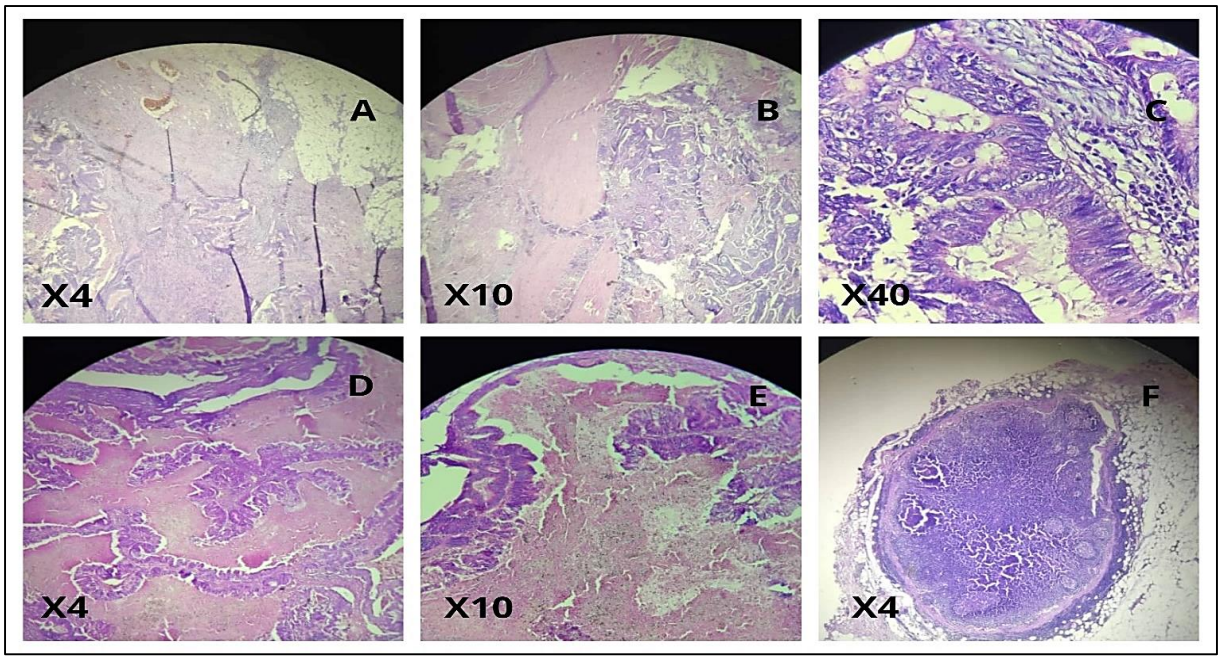

Figure 45. **A)** At low magnification, the tumor infiltrates the colonic wall up to the serosa; **B)** At medium magnification, a photo showing infiltration of the muscular layer; **C)** At high magnification, the tubules are lined by a pseudostratified epithelium with reduced mucosecretion and atypical nuclei; **D-E)** necrosis areas; **F)** A non-metastatic lymph node.

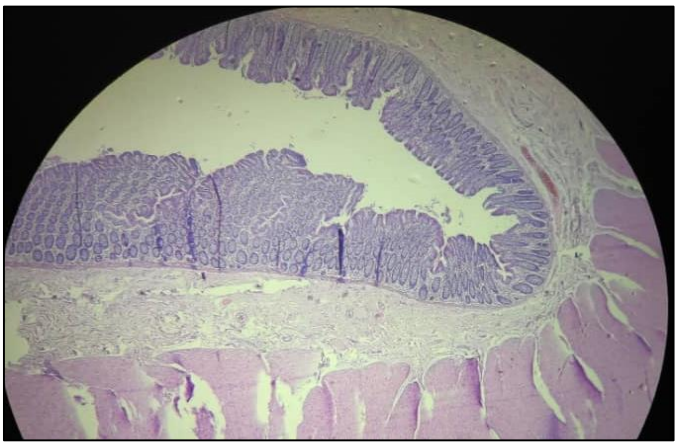

Figure 46. Normal margin.

B. Patient N°2

-Classified as **T4b Nx Mx** based on the TNM staging system, it is also a **moderately differentiated adenocarcinoma (ADK)**. In this case, the microscopy results revealed a colon adenocarcinoma on the basis of the presence of tubular structures with branching papillae on the surface. Additionally, the tumor infiltrates the left ovary, the small intestine, extending up to the serosa. No vascular emboli are observed. **One metastatic lymph node** was identified, indicating the spread of the tumor (1/6). These findings highlight the aggressive nature and extensive local and distant involvement of the tumor.

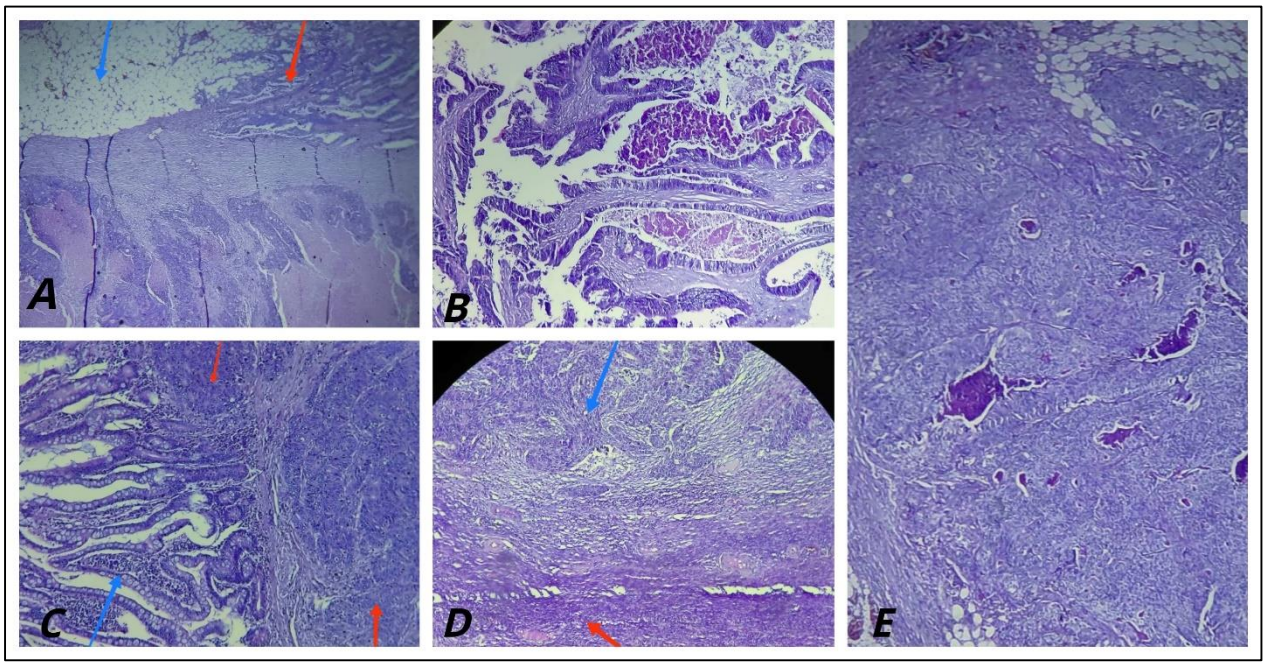

Figure 47. A) Infiltration of the serosa (blue arrow) by the tumor (red arrow); **B)** Papillary architecture at medium magnification; **C)** Infiltration of the ileal wall (blue arrow) by the tumor (red arrows); **D)** Infiltration of the left ovary (red arrow) by the tumor (blue arrow); **E)** A metastatic lymph node Gx10.

- **Immunohistochemistry results**

The immunohistochemical study conducted on the tumor of the left ovary to confirm its colonic origin revealed negativity for CK7, and positivity for CK20, and CDX2.

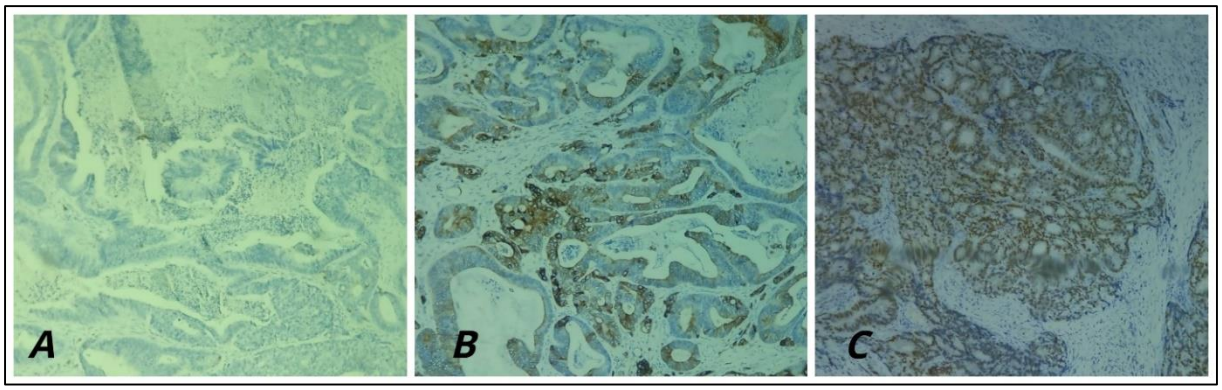

Figure 48. A) adenocarcinoma, negative staining for CK7; **B)** focal cytoplasmic staining for CK20, and **C)** positive nuclear staining for CDX2.

3. Discussion

We conducted a retrospective epidemiological and anatomopathological study in the Department of Anatomopathology of CHU at Constantine, over a period of 3 years. The study involved 60 patients: 23 women and 37 men. These cases were mainly referred by various departments, with a small portion coming from different peripheral sectors. Since the CHU serves as a regional referral center, there is a higher number of samples collected from patients who are hospitalized compared to those who receive outpatient treatment.

The results of our study indicate that there is a higher proportion of men, with a percentage 62% greater than that of women 38%. These findings are aligned with **Bekouaci et Smaili. (2019)** research conducted by the medical oncology department in Blida, located in northern Algeria, which reported 55.6% of men and 44.3% of women. Similarly, **Keraria et al. (2020)** results were obtained from an Algerian study on 31 cases of CRC, which reported a rate of 54.8% for men.

We also observed that the incidence of CRC is proportional to age, with a higher number of cases occurring in older age groups. In this regard, the majority of patients in our study sample were over 60 years old, followed by patients aged between 40 and sixty 60 years old, with relatively significant incidence rates. Finally, we have the cases of patients aged between twenty (20) and forty (40) years old, which represent the lowest rates in the studied period. Several findings were documented by **Araghi et al. (2019)** in 7 developed countries, indicating a higher occurrence of colorectal cancer among individuals over the age of 50 which is in agreement with our results. This finding could be attributed to lifestyle patterns and the influence of various factors, particularly dietary habits **Amani et al. (2022).**

In our study, the most common tumor site was the rectum (28%), followed by the sigmoid colon (18%), thus supporting the data from our literature review "**Epidemiological Data about the Location";** The majority of tumors are situated in the rectum (37%) and sigmoid colon (31%). However, **Mallem (2010)** shows that sigmoid colon cancer occupies the first place. Moreover, we were able to show that rectal cancer was more diagnosed than colonic cancer. These findings are consistent with those of **Siegel (2023), and El Housse et al. (2015),** who reported a predominance of rectal cancer occurrence in comparison with colonic cancer.

Besides, adenocarcinoma was the histological type predominantly diagnosed, with a percentage of 94% during the last three years, which correlates with the studies conducted by **Hakami et al. (2020)** and **Boudemia et al. (2019)** where adenocarcinoma was the predominant histological type.

According to the results obtained during the study period, the majority of tumors were well differentiated (70%), followed by moderately differentiated tumors (25%) and poorly differentiated (5%), thus supporting the findings of **Hamdouche (2016)** in the same department of anatomopathology which reported 89.19% of cases with well-differentiated grades in an older population, whereas poorly differentiated tumors were relatively rare (1,67%).

In our study series, the most common tumor stage among patients with CRC was stage PT3, with 84% of the studied cases. Therefore, the majority of patients were diagnosed in advanced stages, which is consistent with the findings of **Hamdouche (2016)** in the same department of anatomopathology This can be explained by the negligence of symptoms by patients until the cancer reaches an advanced stage in the body.

The evaluation of the expression patterns of CK7, CK20, and CDX2 in the characterization and classification of colorectal cancer (CRC), revealed a significant pattern of CK7 negativity, and positivity in both CK20 and CDX2 in the examined CRC samples. These results are in concordance with **AIlieva et al. (2022)** work**,** which also demonstrated a high proportion of colorectal carcinomas exhibiting CK20 positivity and CK7 negativity. Additionally, the same group of research reported that the majority of colorectal carcinomas showed positive staining for CDX2, with a significant correlation established between CDX2 expression, histologic grade, and tumor invasion depth. This combination of markers contributes to the distinction of CRC from other malignancies and supports the accurate diagnosis of colorectal origin. Further research is necessary to validate these findings and explore their potential impact on CRC management.

Conclusions and perspectives

Cancer is a disease that has become increasingly prevalent in modern times, and colorectal cancer is particularly concerning due to its high frequency, severity, and mortality. It has become a significant public health issue in Algeria, as the incidence of cancer is rising significantly based on data from the National Institute of Public Health and the results obtained from our study conducted at the Department of Pathological Anatomy and Cytology with a ratio of 1,6. This alarming situation prompted us to select colorectal cancer as the focus of our study.

When examining the epidemiological aspects, colorectal cancer tends to occur at a later age, although there are cases where it can manifest at an earlier stage. Additionally, there is a slight male predominance in its occurrence with an average age of 61 years in our study.

Colorectal cancer manifests observable symptoms such as constipation, rectal bleeding, and abdominal pain, both clinically and anatomopathologically. The most frequently affected site is the rectum, which is followed by the sigmoid and is predominately impacted by well-differentiated adenocarcinomas.

To confirm and characterize tumor types, biopsies are routinely performed and a histological analysis is conducted after examining the samples macroscopically and microscopically. The management of colorectal cancer is guided by internationally recognized classifications such as those provided by the World Health Organization (WHO) and the TNM staging system, which allow for a consensus on treatment approaches. While anatomopathological and histological techniques play a crucial role in diagnosis, the combination of these techniques with molecular methods offers greater accuracy and precision in determining the molecular subtype of colorectal cancer. This information is instrumental in selecting the most appropriate treatment, as certain treatment options may be influenced by the specific molecular characteristics of the cancer.

From a perspective, CRC may provide a clinical model for studying preventive vaccination approaches, particularly for hereditary forms, which represent one of the promising therapeutic perspectives.

Appendices

RAPPORT DE STAGE

Nom/Prénom : BERKANE Amira

HIRECHE Djoumana

Formation : *L'extraction des huiles essentielles*

Année : *2022 /2023*

Entreprise : *Unité de Recherche Valorisation des Ressources Naturelles Molécules Bioactives et Analyses Physico-Chimiques et Biologiques, Departement de Chimie, Facult é s des Sciences Exactes, Universit é de Constantine 1, Algérie.*

Tuteur de stage : *Dr Redouane Lemoui*

1. INTRODUCTION

L'extraction d'une huile essentielle (HE) est un processus sophistiqué et délicat. Son objectif est de capter et d'extraire les composés végétaux les plus volatils, les plus nuancés et les plus délicats sans en altérer la qualité. Pour mesurer la complexité de la tâche, considérons la rapidité avec laquelle le parfum d'une fleur, même la plus odorante, se pose, puis se dissipe ou se déforme lorsque ses pétales se replient. L'essence s'échappe et de nombreuses molécules odorantes se dispersent dans l'air ambiant lorsque la cuticule cireuse des compartiments épidermiques est rompue.

2. MÉTHODES D'EXTRACTION DES HUILES ESSENTIELLES

- **Préparation des plantes** les plantes collectées doivent être préparées avant l'extraction. Cela peut inclure le nettoyage pour éliminer les impuretés telles que la terre ou les résidus, et le séchage pour réduire la teneur en eau. Dans certains cas, les plantes peuvent être broyées ou coupées en petits morceaux pour faciliter l'extraction.

Il existe différentes méthodes d'extraction des plantes, notamment l'extraction par distillation à la vapeur, l'extraction par solvant, l'extraction par pression à froid, l'extraction par macération, etc.

- **L'extraction par distillation à la vapeur** il consiste à faire passer un courant de vapeur d'eau dans une cuve contenant les plantes. Sous l'action de l'humidité et de la chaleur, les huiles essentielles volatiles se libèrent. Ensuite, cette vapeur d'eau et d'huile essentielle passe dans un serpentin refroidi par l'eau. La vapeur se condense alors dans le serpentin, et retourne à l'état liquide. Ce liquide, mélange d'eau et d'huile essentielle est recueilli dans un essencier qui sépare les deux éléments. En effet, l'huile essentielle est non miscible à l'eau et plus légère donc elle se retrouve dans la partie supérieure.

Figure 1. L'appareil d’extraction par distillation à la vapeur

- **L’extraction par solvant** cette méthode est utilisée pour obtenir des huiles florales très parfumées. Les plantes et le solvant sont placés dans un récipient et chauffés pour faciliter l'extraction des huiles par le solvant. Le mélange résultant est ensuite filtré et devient ce que l'on appelle le "concret", qui est ensuite mélangé avec de l'alcool, refroidi et filtré. Suite à l'évaporation de l'alcool, il reste une huile très parfumée dite "absolue”
.

Figure 2. L'appareil d’extraction par solvent.

- **L'extraction par pression à froid** cette technique s'applique aux huiles citronnées et agrumes (comme le citron, l'orange, la mandarine). Les écorces ou les zestes sont pressés par une machine ou à la main pour en débarrasser les huiles. L'extrait alors recueilli se nomme « essence aromatique » et non « huile essentielle » car il n'y a aucune modification chimique.

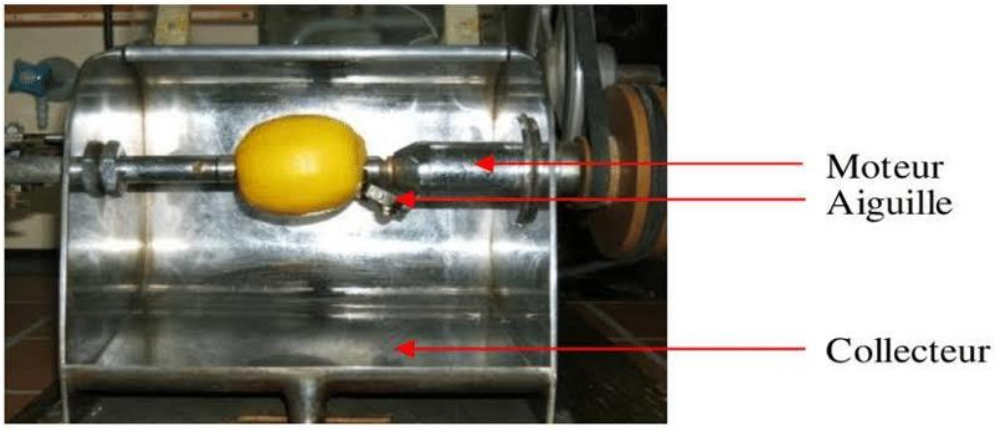

Figure 3. Schéma de montage de l’expression à froid (78).

- **L'extraction par macération** est un procédé qui consiste à laisser séjourner un solide dans un liquide froid pour en extraire les composés solubles, ou bien pour qu'il absorbe ce liquide afin d'en obtenir le parfum ou un arôme pour le préserver ou le dégrader.

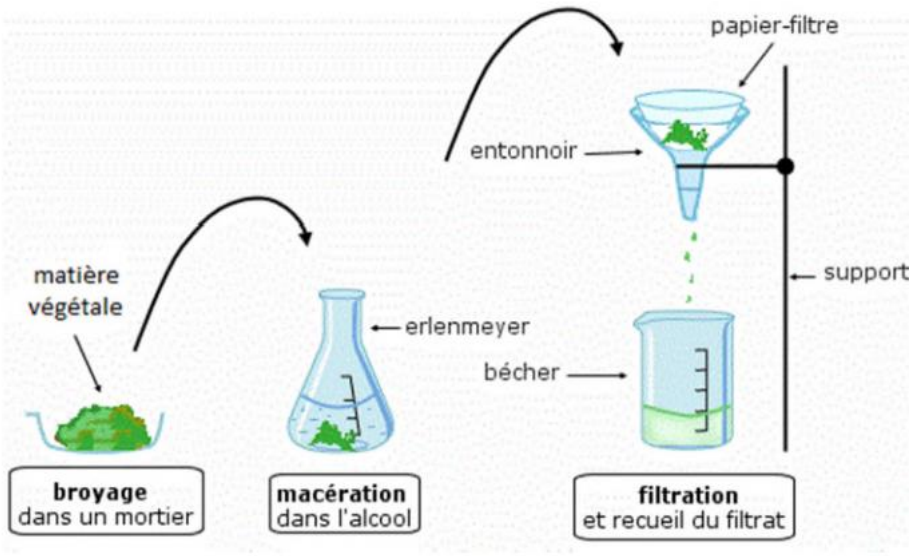

Figure 4. Schéma d'un montage de macération.

- **La chromatographie sur couche mince** est une technique de séparation des ingrédients d'un mélange homogène. Il sert à identifier ces ingrédients en les comparant à une référence ou à certifier la pureté d'un produit. Si les espèces à étudier ne sont pas visibles, une étape de révélation doit être effectuée. La plaque chromatographique est placée dans une cuve d'élution avec éluant. Lors de l'élution, celle-ci remonte le long du plateau et entraîne les nombreux constituants, chacun à son rythme propre déterminé par la nature du constituant et de l'éluant. A la fin de l'analyse, sur la plaque, les constituants qui seront en haut de la plaque auront été peu retenus par la plaque de silice et bien emportés par l'éluant (bonne affinité) et inversement. Le résultat obtenu est appelé le chromatogramme.

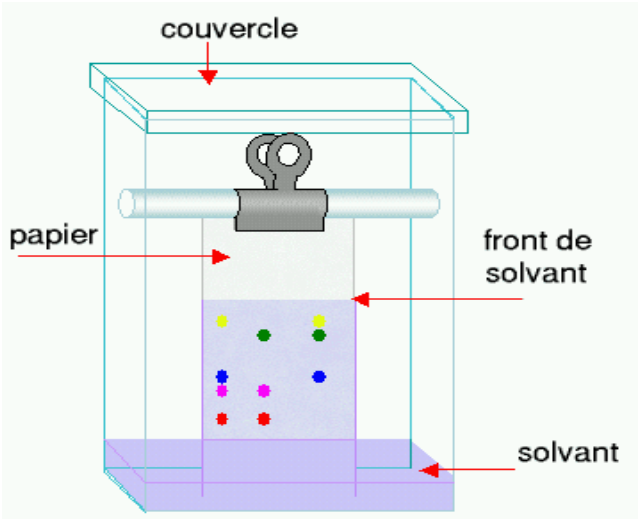

Figure 5. Schéma d'une chromatographie sur papier (50).

3. CONCLUSION

En somme, l'extraction des HE de la matière végétale peut être réalisée au moyen de plusieurs procédés, basés sur des techniques anciennes ou récentes. Cependant, quel que soit le procédé utilisé, l'extrait final correspond à une concentration des composés initialement présents dans la matière première. De plus, les méthodes de production tout comme l'origine géographique, le climat, le sol, la période de récolte ou bien encore les pratiques agriculturales, peuvent avoir une influence directe sur la composition chimique de l'huile essentielle distillée.

BERKANE Amira

HIRECHE Djoumana

[Frères Mentouri Constantine 1university]

[2022-2023]

Internship Report at the CHU of Constantine About an Epidemiological and Anatomopathological Study of Colorectal Cancer

Abstract:

The following report provides an overview of a thesis conducted at CHU Constantine in the Department of Anatomic Pathology. The thesis focused on the epidemiological and anatomopathological study of colorectal cancer. This report summarizes the objectives, methods, results, and discussion of the study, highlighting the key findings and their implications for the prevention, diagnosis, and treatment of colorectal cancer.

1. Introduction:

Colorectal cancer is a significant global health burden, accounting for a substantial number of cancer-related deaths worldwide. It is crucial to conduct comprehensive studies to understand the epidemiological and anatomopathological aspects of this disease. The Department of Anapath at CHU Constantine recognizes the importance of such research in improving prevention, early detection, and treatment strategies for colorectal cancer. This thesis aims to contribute to the existing knowledge base by conducting an in-depth epidemiological and anatomopathological study of colorectal cancer within the study population.

2. Objectives:

Objectives: The objectives of this thesis are as follows:

1. To determine the epidemiological characteristics of colorectal cancer cases in the study population at CHU Constantine.
    - This objective involves examining the incidence and prevalence rates of colorectal cancer, as well as analyzing demographic and clinical factors associated with the disease.

2. To investigate the anatomopathological features of colorectal cancer samples.
    - This objective entails conducting a detailed analysis of tissue samples obtained from colorectal cancer patients, examining histopathological characteristics, tumor staging, and molecular markers.
3. To identify potential correlations between epidemiological and anatomopathological findings.
    - This objective aims to explore possible associations between specific epidemiological factors (such as age, gender, and lifestyle) and the anatomopathological characteristics of colorectal cancer, providing insights into disease progression and prognosis.
4. To contribute to the existing knowledge base and inform clinical practice.
    - This objective involves interpreting the study findings in the context of current literature and discussing the implications for diagnostic accuracy, treatment selection, and preventive measures. The research outcomes will be valuable in guiding evidence-based decision-making in colorectal cancer management.

By addressing these objectives, this thesis endeavors to enhance our understanding of colorectal cancer and pave the way for improved strategies in its prevention, early detection, and treatment at CHU Constantine.

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Abstracts

الملخص

سرطان القولون والمستقيم يعتبر من بين أكثر أنواع السرطان شيوعًا في العالم (بعد سرطان الثدي وسرطان البروستاتا). أحد (CRC) ومع ذلك، فإن معدل حدوثه في بلدنا أقل من تلك الموجودة في الدول الغربية. يُعد سرطان القولون والمستقيم أفضل الأمثلة على تكوّن السرطان عبر خطوات متعددة. ستؤثر معرفة الخصائص الجسمية والمرضية لسرطان القولون والمستقيم بالتأكيد على نهجنا العلاجي. أجرينا دراسة وبائية وتشريحية استعادية في قسم علم وظائف الأعضاء في مستشفى الجامعة بقسنطينة على مدار 3 سنوات. شملت الدراسة 60 مريضًا: 23 امرأة و 37 رجل. هدفت هذه الدراسة إلى تحليل الملف الوبائي والخصائص التشريحية لسرطان القولون والمستقيم. كشفت النتائج التي تم الحصول عليها عن تفوق طفيف للرجال بنسبة 62%. كشفت هذه الدراسة عن تكرر عال للتورم الخبيث في المستقيم (28%) مقارنةً بأجزاء أخرى من القولون. من الناحية النسيجية، أشارت الدراسة السيتوباثولوجية إلى أن الغدة الليفية التمثيلية الجيدة كانت الجانب التشريحي الأكثر تمثيلية في 60 حالة، مما يشكل 70% من السكان المدروسين

لقد شهد سرطان القولون تقدمات هائلة في مجال التشخيص، مثل تقنيات علم الأحياء الجزيئية لاكتشاف عوامل الاختبار لذلك، سيكون من المثير للاهتمام إجراء مسح غذائي لتحديد الدور الهام للنظام الغذائي في وجود هذا .(KRAS ،BRAF) النوع من السرطان. ستكون من ذو فائدة تنفيذ برنامج لفحص الشاشة الشاملة للأفراد الذين تتراوح أعمارهم بين 50 و 80 عامًا وإجراء اختبار الهيموكولت (لاكتشاف الدم المخفي في البراز) كل سنتين.

Academic year: 2022-2023	**Presented by:** BERKANE Amira HIRECHE Djoumana

A retro-epidemiological, Ana-pathological study of Colorectal Cancer in the period of 2020-2022

A thesis submitted for the obtention of a Master degree in Molecular and Cellular Immunology

Colorectal cancer is classified among the most common cancers in the world (after breast cancer and prostate cancer). However, its incidence in our country is lower than that of Western countries. Colorectal cancer (CRC) is one of the best examples of multistep carcinogenesis. Knowing the anatomopathological characteristics of CRC will certainly affect our therapeutic approaches. We conducted a retrospective epidemiological and anatomopathological study in the Department of Anatomopathology of CHU at Constantine, over a period of 3 years. The study involved 60 patients: 23 women and 37 men. This study aimed to analyze the epidemiological profile and the anatomopathological features of colorectal cancers. The results obtained revealed a slight male predominance of 62%. This study identified a high frequency of malignant involvement in the rectum (28%) compared to other parts of the colon. Histologically, the cytopathological study indicated that well-differentiated adenocarcinoma was the most representative histological aspect in 60 cases, accounting for 70% of the studied population.

Colorectal cancer has made tremendous advances in terms of diagnosis, such as molecular biology techniques for biomarker detection (KRAS, BRAF). Therefore, it would be interesting to conduct a nutritional survey to determine the significant role of diet in the etiology of this type of cancer. Implementing a mass screening program for individuals aged 50-80 and conducting an Hemoccult test (to detect occult blood in the stool) every two years throughout our country would be beneficial.

Keywords: colorectal cancer, anatomopathologycal, epidemiological, adenocarcinoma, etiology, screening.

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