Micro-reviews in Cell and Molecular Biology 2021

An Exploration of Current and Future Diagnostics, Treatments, and Preventative Care for Colon Cancer

Author: Savannah G. Beakley
Major: Cell and Molecular Biology
Minor: Marketing
Department of Microbiology and Molecular Genetics, Oklahoma State University, Stillwater, OK 74078, USA

Key Words:
Colon Cancer, Metastatic Colon Cancer, Biomarkers,

As of 2019, one of the largest instances of cancer is that of the Digestive system, with nearly 30% being accounted for by colon cancer (ACS 2019). Colon and Colorectal cancer can be highly metastatic, in which cases it can reduce the five-year survival rate from 90% (localized tumor) to 10% (metastatic progression). Current treatments have negative side-effects and do not always reduce instance of relapse. This review will explore and compare current treatments, diagnostic techniques, and preventative measures, as well as the advances in each field relating to colon cancer.

Introduction

Colon and Colorectal cancer was responsible for over 576,000 and 935,000 deaths in 2020, respectively, with over fifty percent of incidence occurring in countries of categorically very high Human Development Index). This makes colon cancer the fourth leading cause of known cancers and cancer-related deaths (WHO, Globocan 2020). This high rate of cancer targeting highly developed countries sparks a need for research and new treatment and prevention options as its prevalence may increase worldwide with the development of other countries.

Colon cancer can be highly metastatic with possible incidence at early stages in disease progression (Hu 2020). The first organ colon cancer usually metastasizes to is the liver, very few are eligible for resurrection and are usually placed on transplant lists (Lui 2003). Metastasis to important organs plays a large role in the mortality rate of colon cancer. Additionally, age and gender play a role in general prognostics with the greatest age risk between 45 and 70 years, and males accounting for 52% of all case and deaths (NIH SEERS 2021). Furthermore, up to one third of colorectal cancer incidence may become hereditary (NCCN 2009) .

The severity and pathogenesis of colon cancer is highly dependent on anatomic orientation and is identified as being left or right sided during diagnosis. These two morphologies of the disease are not always susceptible to the same treatments, meaning different approaches to cancer of the same tissue are required, based upon the anatomical location of tumors developed (Baran 2018).

Current treatments for colon cancer generally include surgery, radiation, chemotherapy, and

immunotherapy all of which are dependent on tumor stage and orientation.

Symptoms and Diagnosis

Symptoms of colon cancer usually include abdominal or stomach pain, severe constipation (this may indicate blockage), bloody stool or rectum, and weight loss. Colon cancer is diagnosed most commonly by colonoscopy. While blood tests cannot effectively determine if cancer is present, they can be used to detect tumor markers in serum after colonoscopy confirms cancer (Mayo Clinic 2018) . In cases where a colonoscopy may be considered invasive, a CT scan may be used to identify any unusual masses, after which a colonoscopy may be performed, or surgery may be scheduled depending on stage severity. Staging of colon cancers is standard where I identify a small non-metastatic tumor, II indicating medium tumor size, III indicating metastasis to proximal organs like nearby lymph nodes or the peritoneal region, and IV indicating metastasis from colon to distal organs such as the liver and lungs (Chowhurdy). Right-sided colon cancer (RCRC) most often appear flat while left-sided tumors (LCRC) often appear as multiple polyps on the inside of the colon and are easier to detect. Diagnosis of right sided tumors can be difficult due to the morphology; in addition, these are typically more aggressive and may secrete mucus and induce inflammatory immune responses. Furthermore RCRC typically have worse prognosis and can metastasize in the abdominal region. LCRC, being easier to detect, are easier to treat, however can often spread to the liver and in severe cases metastasize to the lungs (Baran 2018)

Present Treatment and Results

After a colonoscopy is performed and identifies cancer, biomarkers for the tumor may be used to identify the genetic mutation at fault. CEA or Carcinoembryonic antigen is one of the main biomarkers used in colon cancer treatment. It is often expressed by epithelial tissues during cancer and released into serum, the levels of CEA are measured at the time of diagnostic and are monitored during treatment for comparative analysis. If the levels significantly decrease during the course of treatment, that is indicatory the treatment is likely successful, these levels are continually monitored if the patient reaches remission, as a means of early detection of relapse. However, CEA does not always present in significant amounts and efficacy may be limited on a patient-to-patient basis. TPS, tissue polypeptide specific antigen, is another useful tumor marker. TPS is a proliferation marker of which high level in serum indicate active tumor growth and are correlated with metastasis. If a tumor at early stage is showing probability of metastatic activity, TPS can be used to help monitor growth and treatment results (Jelski 2020). Additionally a variety of growth-associated cytokines such as GM-CSF (granulocyte-macrophage colony stimulating factor) can be used to identify immune inflammation which is often increased as the body defends itself against the tumor growth Once Diagnostics are made, a patient-specific treatment plan is made to target the tumor. Metastatic cancers are associated with drug resistance, and late-stage diagnostics typically result in immediate surgeries (Hu 2020). Once the tumor(s) are either surgically removed or reduced, secondary treatment route is determined. Earl- stage diagnostics and treatments have the best prognosis. If small polyploidy cancers are found during colonoscopy, they may be removed at the time of screening. If this is the case the patients' tumors are sent for histology analysis to determine the tumor type. Most LCRC are susceptible to treatment by chemotherapy. Current chemotherapies that are commonly used include 5-Fluorouracil, Irinotecan, Oxaliplatin, and Trifluridine. Each has a similar mechanism of targeting cells with markers of fast proliferation. While this does target the cancer cells, it can inadvertently damage proliferating

immune cells or cells in the gut epithelium that typically proliferate at a higher rate than many other cells du to their environment. This somewhat non-specific targeting can cause negative side-effects making the patients' recovery painful. Radiation therapy is often a used in addition to chemotherapy and can target cells more specifically using similar markers. A more promising device for treatment is immunotherapy. Currently immunotherapy treatments are more expensive than chemotherapy and radiation but can be more accurate and yield fewer negative side-effects. Car-T is an immunotherapy that can be used in cases where the T cells are mutated and unable to effectively kill cancer cells. Another form of immunotherapy, which is highly specific, is the use on mon-clonal antibodies. In some cases of cancer, cells are mutated to produce antigens that signal downregulation of the immune system. Bevacizumab is an approved immunotherapeutic that targets vascular endothelial growth factor and is used combination with chemotherapeutic agents for early-stage colon cancer. There are currently many monoclonal antibodies being used in late-stage cancer trials with promising results.

Recent Progress

Novel cell markers for future targeting by immunotherapy are currently being researched. Cheng et al found a biomarker in the form of a microRNA with similar detectability to CEA. Their study showed this could be auseful tool in diagnosing cancer and understanding progression better than using CEA markers alone. Additionally more research can be done to understand this interaction with cancer cells for future immunotherapy targets. Another study found that a specific stem cell called LgR5 contributes directly to metastasis of colon cancer. In this study they depleted this cell line in mice before and after cancer incidence, and while there was no significant regression in the tumor after removal, the tumor growth ceased. In the future, studies could look at targeting these stem cells during chemotherapy treatment to reduce active growth and lead to a better patient prognosis (Melo 2017)

Risk and Prevention

The most at-risk groups for colon cancer are those between the ages of 45 and 75 with a family history of the disease. Genetics cannot always be altered, but environmental stimuli that can increase the risk of disease may. Colon and Colorectal cancers are far more prevalent in developed countries, indicating a variety of common factors may contribute to disease risk. These include, but are not limited to, diet, pollution, and drug use. Since LCRC is metastatic to the lungs, it is noteworthy that those with prior history of smoking may be more at risk for developing colon cancer given the lung and colon tissue similarities. This was also found to be true in a 2004 study the gene mutation CYP1A1 in colon cancer was linked to cigarette use.

The best current means of prevention are healthy life-style based.

Discussion

While incidence and mortality rate of colon cancer has greatly decreased in the past three decades, it remains the fourth most prevalent cancer. We can use data and statistics to evaluate risks and make them known to the public to hopefully reduce incidence. Campaigning for better diet, disuse of tobacco products, and early screening could be valuable in preventing incidence of colon cancer in the future. Advances in medicine including genetic and immunotherapies could play a role in reducing mortality rates of late-stage cancers and increase the remission survival rate in the future.

References

Shroeder, Insa S. "Potential of Pluripotent Stem Cells for Diabetes Therapy". Current Diabetes Reports. 5 (2012): 490-498.template

American Cancer Society. Cancer Facts and Figures 2019. Atlanta: American Cancer Society; (2019)

The Journal of the National Comprehensive Cancer Network, "Colon Cancer: Clinical Practice Guidelines in Oncology" Volume 7 Number 8 (2009)

Kory W.Jasperson, Thérèse M.Tuohy, Deborah W.Neklason, Randall W.Burt "Hereditary and Familial Colon Cancer." Gastroenterology: Colon Cancer: An Update and Future Directions. Volume 138, Issue 6 (May 2010): 2044-2058

Felipe de Sousa e Melo, Antonina V. Kurtova, Jonathan M. Harnoss, Noelyn Kljavin, Joerg D. Hoeck, Jeffrey Hung, Jeffrey Eastham Anderson, Elaine E. Storm, Zora Modrusan, Hartmut Koeppen, Gerrit J. P. Dijkgraaf, Robert Piskol & Frederic J. de Sauvage "A Distinct Role for Lgr5+ Stem Cells in Primary and Metastatic Colon Cancer." Nature Volume 543 (2017) 676-680

Tin Wui Wong, Gaia Colombo & Fabio Sonvico "Pectin Matrix as Oral Drug Delivery Vehicle for Colon Cancer Treatment." AAPS: PharmSciTech 12 (2011) 201-214

Hanyin Cheng ,Lina Zhang ,David E. Cogdell,Hong Zheng,Aaron J. Schetter,Matti Nykter,Curtis C. Harris,Kexin Chen ,Stanley R. Hamilton ,Wei Zhang "Circulating Plasma MiR-141 Is a Novel Biomarker for Metastatic Colon Cancer and Predicts Poor Prognosis" PLOS ONE 6(3): e17745

Baran B, Mert Ozupek N, Yerli Tetik N, Acar E, Bekcioglu O, Baskin Y. "Difference Between Left-Sided and Right-Sided Colorectal Cancer: A Focused Review of Literature." *Gastroenterology Research* 2018;11(4):264-273. doi:10.14740/gr1062w

Chowdhury, Reezwana. "Colon Cancer: Diagnosis and Staging." *Johns Hopkins Medicine*, www.hopkinsmedicine.org/health/conditions-and-diseases/colon-cancer/colon-cancer-diagnosis-and-staging.

"Colon Cancer." *Mayo Clinic*, Mayo Foundation for Medical Education and Research, 16 Mar. 2021, www.mayoclinic.org/diseases-conditions/colon-cancer/symptoms-causes/syc-20353669.

Martha L. Slattery, W. Samowtiz, K. Ma, M. Murtaugh, C. Sweeney, T. R. Levin, S. Neuhausen, *CYP1A1*, Cigarette Smoking, and Colon and Rectal Cancer, *American Journal of Epidemiology*, Volume 160, Issue 9, 1 November 2004, Pages 842–852

