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GASTRIC CANCER AS GLOBAL CHALLENGE -A REVIEW

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1. INTRODUCTION

According to the World Health Organization (WHO), International Agency for Research on Cancer, there are more than 940,000 new cases of colorectal cancer diagnosed each year worldwide. This figure may be used to compare with the current population of a country to show how prevalent this disease is. WHO also stated that the highest colorectal cancer incidence rates are found in Europe, the United States, and Canada. This demonstrates that colon cancer is developed in countries with high living standards and also shows that the more developed a country is, the higher the chance of getting colon cancer. However, incidence rates of colorectal cancer are rapidly rising in Japan and countries in Eastern Europe. This is because the lifestyle of these countries is becoming more westernized.[1] The trend can also be observed through the incidence rates of Japanese Americans, which increased from the first to the second generation. The highest incidence rates of colorectal cancer were found in males from the United States, Slovakia, Hungary, and Denmark, and the highest rates for females were found in New Zealand, Denmark, the Netherlands, and France. This may be due to the diet of the people in these countries as an imbalanced diet and consumption of red processed meat and use of alcohol may lead to an increased risk of colon cancer. This data clearly shows that colon cancer is a disease commonly developed in countries that are more developed or are developing. And it is a disease that may affect anyone around the world.[2] Colon cancer is one of the most perilous cancers and is a malignant tumor found in the inner wall of the colon. It is dangerous because it has no symptoms in the early stages, so it is difficult to detect. Colon cancer may affect mucus, which leads to the damage of cell DNA. However, colon cancer can be treated if detected in the early stages. This is a report on the various aspects of colon cancer.[3] In this report, we will discuss the causes and risk factors of colon cancer, the signs and symptoms, how colon cancer is diagnosed, the various methods of treatment, and the different ways to prevent colon cancer.

2. Understanding Colon Cancer

Colon cancer is a cancer of the large intestine (colon). It often begins with a growth called a polyp inside the colon or rectum. Certain types of polyps may become cancerous. The most common types of colorectal cancer are adenocarcinomas. These tumors start in cells that make mucus to lubricate the inside of the colon and rectum. Colorectal cancer often begins as a growth called a polyp inside the colon or rectum. There are two common types of polyps: adenomas and hyperplastic. Adenomas are considered pre-cancerous and have the potential to develop into cancer. Hyperplastic polyps are more common and are not considered pre-cancerous. Over time, some polyps may turn into cancer. It would take several years for a small polyp to develop into cancer. It's important to have regular screening tests for colorectal cancer. These tests can find polyps or early colorectal cancer, even if there are no symptoms. It is more important to have screening tests if you have a history of colorectal cancer in your family. If colorectal cancer is found at earlier stages, it may be easier to treat.[4]

2.1. Definition of Colon Cancer

Cancer is a term that many people are familiar with, but a disease that few can actually define. Cancer is a group of diseases, which in simplified terms, is simply the result of cells that are unregulated and grow out of control. All cells in one's body are regulated by the genes in the nucleus which act as the "brain" of the cell telling it when to divide, grow, and die. There are certain genes called tumor suppressor genes and oncogenes, which regulate the cell division. When these genes are damaged the cell can replicate without regulation and form a tumor. Tumors can either be benign, which means that they are not cancerous, or malignant, which means that they are cancerous. Benign tumors usually can be removed and in most cases do not grow back, whereas malignant tumors must be removed or destroyed and can be life threatening, because the cells can travel to other parts of the body and create more tumors, a process called metastasis. Now that the nature of a malignant tumor is understood, it can be said that colon cancer is the development of malignant tumor in the large intestine. This disease affects both men and women and is most common in people over the age of 50.[3]

2.2. Risk Factors

Diet is also a large controllable risk factor for colon cancer. Diets that are high in fat and low in calcium, folate, and fiber have been linked to an increased risk of colon cancer. Studies have suggested that people who get lots of physical activity have a lower risk of colon cancer. On the other hand, some researchers believe that sitting for long periods of time increases the risk.[5]

Another uncontrollable risk factor is family history. It is estimated that about 20-25% of people who develop colon cancer have a family history of it. If a person has a history of colon cancer in their family, particularly if a first-degree relative developed the disease (parents, siblings, children) at an early age, they are at a higher risk of developing it themselves. In addition to the family history of colon cancer, there are two hereditary conditions, Familial Adenomatous Polyposis (FAP) and Hereditary Nonpolyposis Colorectal Cancer (HNPCC), that are linked to higher rates of colon cancer.[6]

Age is one of the most important risk factors for colon cancer. More than 90% of people diagnosed with colon cancer are over the age of 50. Colon cancer can occur in younger people, but it happens rarely. A person's risk of colon cancer increases as they get older. This is why the American Cancer Society suggests that starting at the age of 50, individuals should begin regularly screening for colon cancer. If there are other risk factors with age, the doctor might want to start screening earlier. There are many risk factors that increase the chance of developing colon cancer. Many of the risk factors are uncontrollable, such as age, polyps, and family history. Other risk factors include eating habits and having other intestinal disorders.[5]

2.3. Common Symptoms

Though treatment for colon cancer can result in a type of memory loss that affects your daily life, the good news is that this side effect is usually mild, and when memory loss is a sign of serious cognitive impairment, it becomes clear early in the process. This means that if you are functioning well from a cognitive standpoint after treatment for colon cancer, continued memory problems are less likely to be related to the cancer. Memory problems can have many different causes. If you do have serious memory loss that affects your daily life, it's important to get a thorough medical evaluation. This can be an important chapter to close in your cancer experience, both for you and for your loved ones. In many cases, memory problems can be improved with lifestyle changes and certain treatments. But even if some problems persist, there are many strategies you can use to compensate and help you to function as well as possible.[6]

3. Types of Colon Cancer

Gastrointestinal stromal tumors (GISTs) start from specialized cells in the wall of the colon called the interstitial cells of Cajal. These cells are a type of nervous system for the digestive tract that signals the muscles in the colon wall to contract to push digested material from the small intestine. GISTs are very rare and while they can be either benign (not cancer) or malignant (cancer), all have the potential to spread to other parts of the body. The only known cure is surgery to remove the tumor before it spreads. If it does spread, chemotherapy is the only treatment, as GISTs do not respond to radiation treatment.[7]

Carcinoid tumors start from a type of hormone-producing cell in the intestine. Most of these tumors are slow growing and usually of the carcinoid syndrome. This term refers to a group of symptoms that a patient can have when there is a large amount of these hormones released which cause, among other things, a fluttering of the heart, diarrhea, and asthma attacks. The symptoms are generally due to metastases to the liver where these hormones are broken down. The only cure for a carcinoid is surgery, if it has not spread, although there are experimental treatments with certain types of chemotherapy drugs.[8]

The two most common inherited syndromes linked to adenocarcinomas are hereditary nonpolyposis colorectal cancer (HNPCC) and familial adenomatous polyposis (FAP). The most common type of cancer in the colon is adenocarcinoma, which accounts for 96 percent of cases. This term refers to a cancer that begins in cells that secrete mucus to lubricate the inside of the colon and rectum. Adenocarcinomas usually start as a non-cancerous growth called a polyp. Over time, some of these polyps can turn into cancer.[9]

3.1. Adenocarcinomas

Signet Ring Cell Carcinomas: These tumors make up only about 1% of colon cancers. The cells in these tumors are not producing mucus that lines the colon, and the cancer cells in signet ring cell carcinomas do not form glands. These cancer cells displace the mucus producing cells in the colon, and accumulate large mucin droplets. This makes the cancer cells look like signet rings when viewed under a microscope. Signet ring cell carcinomas are usually high grade, which is a sign that the cancer cells are growing and dividing quickly. This type of adenocarcinoma has a poorer prognosis than the other subtypes.[7]

Mucinous Adenocarcinomas: These tumors are made up of cancer cells that produce much mucin, a main component of mucus. Colon cancers that are mucinous are more commonly found in the right side of the colon. Sometimes the mucinous cancer cells can fill the inside of the colon with mucin, which can cause the colon to expand. Regular colonoscopy screenings can usually prevent this situation by catching the mucinous cancer before the colon is filled with mucin.[9]

Most colon cancers are adenocarcinomas. An adenocarcinoma is a cancer that starts in the cells that

line the colon and rectum. These cancers start in glandular cells that make mucus to lubricate the inside of the colon and rectum. When tests of colon tissue are described as adenocarcinoma, the cancer cells have formed glands that look much like the glands found in normal colon lining. There are several subtypes of adenocarcinomas. They are listed below according to how much the cancer cells look like normal colon glands, which can be seen in samples of tissue viewed under a microscope. This difference is called differentiation.[10]

3.2. Carcinoid Tumors

Carcinoid tumors arise from neuroendocrine cells, which are involved in regulating the activities of various organs. They can occur in the colon and rectum and also in the small intestine, stomach, and lung. Most commonly, carcinoid tumors occur in the small intestine. Carcinoid tumors in the colon and rectum are rare, making up less than 5% of all carcinoid tumors. Carcinoid tumors in the colon and rectum grow slowly and may not cause symptoms for many years, at which time the tumor may have already spread to the liver.5 Carcinoid syndrome occurs in less than 10% of patients with carcinoid tumors and only if the tumor has spread to the liver. This is because the liver breaks down the substances released by the carcinoid tumor before they can spread throughout the body. When this occurs, the patient may experience flushing of the face, diarrhea, and difficulty breathing. A rare, but serious symptom of carcinoid tumors occurs when substances released by the carcinoid tumor thicken the lining of the right side of the heart or valves, leading to shortness of breath, a heart murmur, weakness, or heart failure. Unlike carcinoid tumors in the small intestine, which are often diagnosed at an advanced stage, carcinoid tumors in the colon and rectum are usually found during a routine colonoscopy and have not spread. The 5-year survival rate is 90% for carcinoid tumors in the colon and rectum. Treatment for carcinoid tumors in the colon and rectum may include surgery, and sometimes there is a need for more than one operation if the entire tumor could not be removed during the first surgery. If the carcinoid tumor has spread to the liver, other treatments may include cryotherapy, embolization, radiation therapy, or chemotherapy.[11]

3.3. Gastrointestinal Stromal Tumors (GISTs)

The final type of cancer, gastrointestinal stromal tumors (GISTs), are not actually considered a primary colon cancer, but they can spread to the colon and often go undetected because there is no good way to accurately diagnose them. They originate in nerve cells in the wall of the GI tract and can be either benign or malignant. Malignant forms of GISTs can spread to other parts of the body and are very difficult to treat. DNA sequencing has shown that many GISTs have a number of mutations in their DNA that cause cells to be cancerous. These mutations can be inherited and are likely to be present in cases of familial GISTs. GISTs are becoming an increasingly popular topic for clinical research and many clinical trials are available for patients with GISTs. Current studies to treat GISTs and other cancers which start in connective tissues such as bone, fat, muscle, blood vessel, and are known as malignant sarcomas, are exploring selective ways to target the cancer cells. One major trial is using an agent that has been effective in treating other cancers by targeting abnormal proteins in cancer cells. The hope is that selective agents will offer an alternative to older chemotherapy methods which essentially poison all rapidly dividing cells, cancerous or normal.[10]

4. Screening and Early Detection

Having provided a description of colorectal symptoms, we can now move on to the current colorectal screening practice to see how it measures up against the standards discussed in previous sections. Detection of early disease or precursor lesions with a simple, safe, accurate, and acceptable screening test is one of the prerequisites for a successful screening programme. In the case of colorectal cancer, a long 'adenoma-carcinoma sequence' provides a 10-year window in which to detect and remove the precursor lesion before cancer develops. Early detection of cancer or 'curable' disease is the key to improving survival from the disease.5 Up to 90% of people diagnosed with localized colorectal cancer survive 5 years compared with only 10% of those diagnosed after development of metastatic disease. Currently, most colorectal cancers and polyps are detected when patients present with rectal bleeding or change in bowel habit to their general practitioner. Unfortunately, the fecal occult blood test used with the intention of detecting early colorectal cancer actually has a low sensitivity for cancer and is not an effective test for screening. Most positive results are due to upper gastrointestinal bleeding and the test has no impact on detection of advanced adenomas. Although flexible sigmoidoscopy and barium enema are effective tests for detecting cancer and polyps, a recent large UK trial has shown that offering flexible sigmoidoscopy to people between the ages of 55 and 64 reduces colorectal cancer incidence and related deaths by over 50%. Flexible sigmoidoscopy is, however, an uncomfortable procedure which can miss lesions in the right side of the colon.[11]

4.1. Importance of Screening

There are two ways scientists and doctors have found to prevent the onset of colorectal cancer. The first is to remove adenomas during a colonoscopy. Adenomas are non-cancerous tumors which are the precursor to cancer. This discovery was made accidentally when researchers were examining a study on the flexibility of the sigmoidoscope. They found that there was a considerable drop in the rate of colorectal cancer amongst those who had taken part in the study and it was assumed that it was because the adenomas had been removed. A large scale trial then took place to confirm this hypothesis and it was found to be true, with a 76% reduction in fatal colorectal cancer in those that had undergone polypectomy. The removal of adenomas is only relevant to those who

actually have the adenomas in the first place. This leads on to the second method of prevention, which is to screen the population for colorectal cancer. Screening here means testing a seemingly healthy individual to check for signs of a disease, and while there are many possible ways to do this it is not yet clear which would be the most effective for colorectal cancer.[12] An ideal screening test would be one that is non-invasive, easy to do, accurate, and has few possible complications. It would need to detect both the early signs of cancer and also the adenomas which precede it because eradicating them would prevent the onset of the disease. The two most common methods of screening for colorectal cancer are fecal occult blood testing and flexible sigmoidoscopy, which is a less intrusive, shortened form of colonoscopy. This said, the realization of a great reduction in mortality due to effective screening has led to increased advocacy for colonoscopy as the best way forward. This is because colonoscopy has the potential to both detect and remove cancer at one time. The reason why screening the entire population could be the most effective way to prevent colorectal cancer is because of the increase in incidence of the disease with age. It has been seen that while the rate of colorectal cancer has declined in those aged 50 and over, there is a concurrent rise in the younger population. A likely explanation for this is because the precursor to colorectal cancer is common among older people and not easily accessible to study. Hence, it might be more cost-effective to test the younger generation to look for signs of the disease before it becomes a major public health issue. This is because treatment for early colorectal cancer can be less costly and debilitating than advanced cancer, and the detailed study of younger people can lead to a better understanding of how to prevent the disease.[13]

4.2. Colonoscopy

An initial study of colorectal cancer symptoms and early warning signs is carried out by a Digital Rectal Exam (DRE) and a Fecal Occult Blood Test (FOBT). The American Cancer Society recommends that, beginning at age 50, both of these tests should be done annually. One additional method of screening involves a procedure called a flexible sigmoidoscopy. If the results from any of these three tests are positive, a colonoscopy will then be scheduled. A colonoscopy is one of the most sensitive and specific tests for colorectal cancer and it is one of the few screening tests that can also prevent colorectal cancer. If the combination of FOBT and DRE plus flexible sigmoidoscopy are done as a "screening package", it has been shown to reduce colorectal cancer incidence and death. Flexible sigmoidoscopy (a visual inspection of the lower colon and rectum) needs to be recommended more widely. It is cost effective and has accepted complication rates. If adenomatous polyps are not found during the test and have largely been removed, the person does not need to be tested again for 10 years. But if results are positive, the patient should go for a colonoscopy.[14]

4.3. Other Screening Methods

Flexible sigmoidoscopy is similar to colonoscopy, but utilizes a flexible lighted tube to examine only the lower part of the colon. Because the test is less invasive and does not usually require sedation, it is often easier to access than colonoscopy. However, if the flex sig reveals an adenoma or cancer, the patient will need a full colonoscopy. Finally, there are several stool-based tests that are easy and inexpensive to perform, and are effective means of early detection. These include the fecal occult blood test, the guaiac-based fecal occult blood test, and the fecal immunochemical test, all of which test for blood in the stool, as well as the stool DNA test, which checks for abnormal DNA in the cells of the stool. Both positive and negative results for these tests should be followed up with a colonoscopy for confirmation.[15]

Another alternative to colonoscopy is a CT colonography, which utilizes virtual imaging. A CT scan creates detailed cross-sectional images of the body. These images are arranged to show the colon in 2D and 3D format for analysis. While this is an effective means of screening, should suspicious polyps or lesions be located, a standard colonoscopy will then be needed to remove the growth or obtain a biopsy for diagnosis. A variety of other methods can be used to screen for colorectal cancer. These techniques are often used in patients who are unable to undergo colonoscopy or are at a higher risk of complications from colonoscopy. A double contrast barium enema is an x-ray of the colon. During the procedure, a series of x-ray images are taken of the entire colon after the patient is given an enema with a barium solution as well as air.[16]

5. Diagnosis and Staging

Physical examination is the first step to diagnose colon cancer. If one has symptoms such as change in bowel habit, rectal bleeding or abdominal pain, the doctor will perform physical examination including digital rectal examination (DRE) or checking for the presence of blood in feces. But physical examination can pick up only advanced cancer. It means cancer that grows through or into the wall of the colon can sometimes be felt by the doctor during a physical examination. This is often the case if one has a tumor in the right side of the colon. Sometimes the doctor won't do physical examination but directly to the next test which is imaging test. Imaging tests are used when a patient has symptoms or their physical examination suggests that they have cancer. Several types of tests are used to look for the cause of a health problem in the abdomen. The choice of imaging test depends on the patient's symptoms and on whether the doctor suspects colon cancer or another condition. The common imaging tests are chest x-ray, double contrast barium enema (DCBE), computerized tomography (CT) scan and colonoscopy. But in this modern era the more specific imaging test can be used to diagnose colon cancer at earlier stage such as magnetic resonance imaging (MRI) and positron emission

tomography (PET) scan.[17] But these two tests are not widely used in Malaysia and it's quite expensive. All of imaging tests are used to determine whether a suspicious area seen on another test is actually a tumor and to evaluate the extent of spread of the disease. If an imaging test indicates that one might have cancer, a biopsy is usually done to be sure. A patient may also need a biopsy to determine if a suspicious area is cancer, to classify the type of cancer and to grade how far it has advanced. In a biopsy, the doctor removes a piece of tissue from the colon. This is done by colonoscopy or by surgery. A colonoscopy is an endoscopic examination that carries a piece of tissue from the inner the colon using a flexible lighted tube with a small camera on the end. Biopsy is pre-emptive before a patient is done to a treatment in order to reveal the type of cancer and to provide the most appropriate treatment. This is because the type of cancer and how far it has advanced are the most important factors in planning a treatment and assessing the outlook (prognosis).[18]

5.1. Physical Examination

Finally, the doctor may feel your abdomen to check for masses or other abnormal areas. This is usually done if the doctor thinks the patient's symptoms may be caused by something other than cancer. A doctor may also be able to check for ascites, which is a buildup of fluid in the abdomen. This gives the abdomen a swollen and bloated feeling. Depending on the cause and amount of fluid, the swelling can develop very gradually or come on quite suddenly due to severe irritation of the lining of the cavity (peritoneum). Whether the swelling is due to rapid pressure outside the bowel or direct involvement of the serosal surface by the cancer, it is an important sign that the cancer has progressed to an advanced stage.[20]

In addition to a digital rectal exam, the doctor may do a fecal occult blood test. This is a test to check for hidden blood in the stool. Patients collect samples of their stool. Patients should check with their doctor, but generally they need to avoid certain foods and medicines and the doctor may ask them to stop taking iron temporarily. One test involves placing a smear of stool on a card, which is then sent to a doctor's office or a lab. During another test, the patient places a test pad into the stool in the toilet bowl. If the pad changes color, even a little bit, hidden blood may be present. If blood is found, additional tests may be needed. The doctor may also check for blood in the stool by doing a rectal exam with a gloved finger and using a test kit to check for blood in the rectal area. This test is called a fecal immunochemical test. Finally, the patient may be asked to undergo a test with a sigmoidoscope. A sigmoidoscope is a thin, hollow, lighted tube about the thickness of a finger. The doctor will explain what dietary and fluid changes are necessary the day before the exam. During this exam, only the left side of the colon needs to be cleaned out, which is generally easier than doing a full bowel preparation. Any type of sigmoidoscopy requires enemas along with a light breakfast and clear liquids the day before the test. In some tests, the patient may not eat or drink anything the whole day before the test. A liquid diet and laxatives may also be required. In case a mass is found, the doctor will want to do a colonoscopy at another time to check the rest of the colon.[21]

5.2. Imaging Tests

Imaging tests, while not definitive in diagnosis, are useful in determining the right location to take a tissue sample during a biopsy. They are also useful in determining the most appropriate treatment or assessing progress during or after treatment.[22]

MRI scans are becoming more and more useful in detecting colon cancer by providing a better look at the rectum and colon. An advantage of MRI over CT scans is that it does not require exposure to radiation. However, it can also be more costly and can provide less clear images. Both CT scans and MRI scans may require the use of an intravenous or oral contrast, which is a special dye that helps to provide clearer images of certain areas. A contrast enema is an x-ray of the colon and rectum and may be useful in determining whether cancer has invaded through the wall of the colon and into nearby tissues. Imaging tests are an important step towards determining the spread of cancer and determining the stage of colon cancer. A CT (or CAT) scan is a special X-ray test that helps detect a state in which cancer is localized. This test is often used to determine if a colon cancer has spread to the liver or lungs. CT scans are also useful in determining the next step in testing by identifying enlarged lymph nodes that would need to be biopsied. Sometimes a special type of CT scan known as a virtual colonoscopy may be used to screen for the presence of polyps or cancer in the colon. This test is non-invasive so it may be preferred for older patients or those who have other medical conditions that prevent them from having a standard colonoscopy. However, if this test does show an abnormality, a standard colonoscopy would still be required to biopsy or remove any abnormalities. A PET scan is another imaging test that is sometimes useful in detecting whether cancer has spread to other organs.[23]

5.3. Biopsy and Pathology

To confirm the presence of colorectal cancer (CRC), a biopsy must be done. Biopsy is the removal of a small piece of tissue for examination under a microscope. It is the only way to confirm a diagnosis of cancer. For suspected colorectal cancer, the best procedure is to remove the entire growth or tumor in a procedure called resection. This may be the only treatment needed if the disease is found early and the tumor is a very early stage cancer (Tis) or a small polyp. There are many different tests for examining the removed tissue. Most often, the tissue will be looked at with a lighted microscope. Other tests with special tools can be used to examine the patterns of antigens or genes in the tissue which can be useful for predicting the aggressiveness of the cancer or the chance of it recurring.[24]

6. Treatment Options

Chemotherapy is the use of drugs to kill cancer cells. There are many types of chemotherapy drugs. This is often used with surgery for treating colon cancer. Chemotherapy can be given before or after surgery. The aim is the same for both ways, to prevent the cancer from recurring. If chemotherapy is given before surgery, it can shrink the cancer and make its removal easier. If chemotherapy is given after surgery, it can kill any cancer cells that remain in the body. This can lower the chance of the cancer recurring. The goal when treating colon cancer is to remove all the cancer with surgery. If the cancer is found at an early stage, it can be removed during a colonoscopy. If the cancer has grown into the colon, your doctor may recommend a partial colectomy. This is the removal of part of the colon. If the cancer is found at a later stage, your doctor may recommend a colostomy. This is done if it is not possible to rejoin the two ends of the colon after the cancer has been removed.[25]

6.1. Surgery

For most patients with colon cancer, the surgical oncologist is the most important part of the treatment team. Finding a surgeon who has a lot of experience in treating colon cancer can be worth the effort. Studies have shown that patients with colon cancer treated by more experienced surgeons tend to have better results. In some cases, a second operation to resect an anastomosis may be necessary. An anastomosis is the surgical connection of two body parts. This second operation involves re-cutting into the colon at the same location. This procedure may be needed when a leak or a fistula forms, or when the area does not heal. Simple repair of these complications is often not successful and another resection is usually required. This second operation should be performed by an experienced surgeon.[26]

The best way to cure colon cancer is to surgically remove the cancerous part of the colon. This is most effective when the cancer is found early. If the cancer is found early, and is only in the inner layers of the colon, burning the cancer off with electricity (fulguration) or removing it with surgery are often the only treatments needed. If the cancer is found in a polyp and removed while the cancer is in a very early stage, no more treatment may be needed.[27]

6.2. Chemotherapy

There are a number of other writing services that have been doing great in the recent past and one of these papers that you may look at is "5-Fluorouracil and Leucovorin. (1990). GI Cancer Update, 1(2):1-4." This article about chemotherapy discusses what the authors call "the gold standard" in modern adjuvant chemotherapy for colon cancer, a regimen that utilizes 5-fluorouracil (5-FU) and leucovorin. This combination is basically the only treatment that has been found to be effective in improving disease-free and overall survival in colon cancer patients, though numerous attempts have been made to improve on this. This article, in comparison to the previous, is much more technical, and if you choose, you may be able to glean some information on 5-FU treatments that I do not cover in this site from a close reading of the article. This article stands in stark contrast to some of the other resources I refer to on my site in that the tone is very positive, and it seems that the authors believe that the use of 5-FU and leucovorin is a pretty effective treatment for colon cancer. This resource can be a bit difficult to find unless you have access to a medical library because it is a newsletter produced by some cancer center, but if you have access, this is a good opportunity for you to use this resource. To be honest, the addition of this paragraph is mostly a statement on evidence-based medicine (ebm) and how much we rely on the written word for evidence, and it's really not meant to guide you in any direction, but I am consistently surprised by how many people look at my site, so I thought you may like to know about this resource.[28]

6.3. Radiation Therapy

Radiation therapy (also called radiotherapy) uses high energy rays to kill cancer cells. It is an option for treatment for every stage of rectal cancer. In patients with stages II or III rectal cancer, radiation is given before surgery (known as neoadjuvant treatment) to shrink the tumor, making it easier to remove. Combined with chemotherapy, radiation therapy is usually the initial treatment in patients with stage III cancer. This is called chemoradiation. Studies have shown that adding radiation to the treatment plan will increase the chance of the cancer not coming back, making survival rates higher. Patients who have surgery to remove stage II or III rectal cancer will often receive radiation therapy after the surgery if the surgeon feels that there are some cancer cells that were left behind, or if there is a high chance of the cancer coming back. This is called adjuvant treatment, and is done before chemotherapy. It has been shown that patients who have adjuvant radiation therapy have a lower chance of the cancer coming back. For rectal cancer that has either come back or has spread to other parts of the body, radiation therapy can be used to help prevent, relieve or control the symptoms as much as possible. When rectal cancer has spread to the bones, pain can be relieved by radiation treatment to the affected areas. Radiation therapy can also be used to help treat rectal cancer that has spread to the liver and the lungs.[29]

7. Targeted Therapy

Targeted therapy is a type of cancer treatment that uses drugs to specifically identify and attack cancer cells. Targeted therapy is not yet a standard treatment for colorectal cancer, but is being tested in clinical trials. It is being used for advanced colorectal cancer, usually in combination with standard chemotherapy. Targeted therapy consists of drugs that specifically target abnormalities present within the cancer cells. These abnormalities stimulate the uncontrolled growth of

cancer cells and cause the tumor to spread. By focusing on these targets, the drugs do not affect the normal cells and usually cause fewer side effects than chemotherapy. There are two types of targeted drugs used for the treatment of colorectal cancer which are monoclonal antibodies and small molecule drugs. Monoclonal antibodies are given through a drip in the arm which attacks the protein on the outside of the cancer cells. Small molecule drugs are taken in the form of tablets and work by attacking the abnormalities within the cancer cells. Both types of targeted drugs are usually taken in combination with standard chemotherapy. Monoclonal antibodies given for colorectal cancer targeted therapy are bevacizumab, cetuximab and panitumumab. Bevacizumab is used for advanced colorectal cancer and for the treatment of recurrent colorectal cancer. It is often used in combination with chemotherapy and is also being tested to see if it can prevent the recurrence of cancer after surgery. Cetuximab and panitumumab are used for the treatment of advanced colorectal cancer and for the reduction of symptoms in patients who are no longer responding with irinotecan and oxaliplatin chemotherapy. These monoclonal antibodies have been shown to help the survival rates of patients with advanced cancer and have been proven beneficial for the improvement of cancer symptoms. Small molecule drugs given for colorectal cancer targeted therapy are regorafenib and the cancer drugs, which can be taken as tablets before being absorbed into the bloodstream. Regorafenib is used for advanced colorectal cancer and for the treatment of patients with a tumor that cannot be removed with surgery. It is prescribed after other treatments have been unsuccessful and is usually taken in combination with the cancer drug as tablets. This targeted therapy has only recently been developed and therefore is currently being tested to see how effective regorafenib is and to confirm whether it is safe to use for colorectal cancer.[30]

7.1. Overview of Targeted Therapy

Targeted therapy is a newer approach to cancer treatment that has been developed over the past 10 years. It is a cancer treatment that uses drugs to identify and attack specific cancer cells. It is different from traditional chemotherapy in that it specifically targets cancer cells and does not damage normal cells. Targeted therapy works by using drugs to block the growth and spread of cancer by preventing the cancer cells from dividing or by destroying them directly. It targets the changes in the cancer cells that help them divide, grow, and spread. This is in contrast to traditional chemotherapy which directly affects cancer cells as well as normal cells. Targeted therapy has very different side effects than chemotherapy because it affects only cancer cells and does not harm normal cells.[31]

7.2. Types of Targeted Drugs

The development of targeted therapies for cancer treatment has followed two main paths. The first path involves identifying the changes within cancer cells that are driving the cells to grow and divide uncontrollably (i.e. the mutations), discovering the proteins that these mutations produce, and developing drugs to inhibit these proteins. The second path is to identify new targets that may be unique to cancer cells, compared to normal cells, and to develop drugs that are directed at these targets. Inhibiting these target proteins may then cause the cancer cells to die, while sparing normal cells. An example of the first approach is the use of the drug bevacizumab to treat colorectal cancer. Bevacizumab is a type of drug known as a monoclonal antibody. Monoclonal antibodies are a relatively new type of targeted therapy which act in a similar way to chemotherapy by targeting specific cancer cells. However, they are different to chemo in that they do not destroy the cancer cells and monoclonal antibodies are usually less likely to harm normal cells. Monoclonal antibodies target specific receptors on the surface of cancer cells. In the case of bevacizumab, the antibody targets a protein known as vascular endothelial growth factor (VEGF) which is involved in the growth of new blood vessels by the tumor to supply itself with nutrients. By preventing this protein from working, the drug starves the cancer cells of nutrients and oxygen, causing them to die. Bevacizumab is typically used in combination with a chemotherapy regime and has been shown to improve the survival of those with colorectal cancer.[32]

7.3. Side Effects and Management

These side effects occur as a result of damage to normal, healthy cells. This can be distressing for patients to cope with as their cancer treatment is apparently making them feel worse. It is can be reassuring to balance this against the fact their cancer is being treated and targeted therapy is usually given for a short time. It is important to let your medical team know if you are experiencing these side effects. They may decide to change your treatment or will be able to provide assistance in managing the symptoms.[32]

- Skin problems - rash and itching - Tiredness - Diarrhea - High blood pressure - Problems with wound healing - Mouth sores.

Targeted drugs cause fewer side effects than standard chemotherapy because they specifically target the cancer cells.

8. Palliative Care and Supportive Treatments

Palliative care is the term given to a form of treatment aimed at easing a patient's symptoms without aiming to cure the disease itself. Its focus is on providing relief from the symptoms, pain and stress of the cancer to improve the overall quality of life. It can often be applied alongside other treatments that are aimed at extending life or curing the cancer. An example of this would be a patient with severe pain from the spread of the cancer to his bones, that is affecting his day to day life. At the same time as receiving chemotherapy to try and shrink the tumor, he may undergo treatment with palliative

radiotherapy to the affected bone. A common misconception is that palliative treatments are only given to patients with terminal cancer, but this is not the case and they are often used to relieve symptoms caused by the cancer in situations where there is still hope of a cure.[31]

When colon cancer is diagnosed in its advanced stage or has spread to other organs, the chances for a full cure are much lower. Despite this, the advanced stages of colon cancer can range from symptomless to severe and in many cases can be relieved by various treatments. The aim of treatment in this situation is to extend life and improve the quality of it despite an inability to eradicate the cancer. In cases where the cancer has spread and is no longer curable with treatment, a patient's condition can often be managed with palliative care and the use of treatments designed to relieve the symptoms that are significantly affecting their quality of life.[34]

8.1. Palliative Care

Palliative care is an approach that improves the quality of life of patients and their families facing the problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial, and spiritual. This is achieved through a holistic approach to care from diagnosis through to end of life and into bereavement. The goal of palliative care is the achievement of the best quality of life for patients and their families. Ideal management encompasses all aspects of patient care and support, which is sensitive to the needs of the patient. This has presently been denoted in the recent publication of the National Cancer Control Programmes in 2005. Palliative care is the responsibility and provided by all healthcare professionals in conjunction with other aspects of the provision of healthcare. As an important aspect of care in all healthcare settings, an understanding of the importance of addressing the needs of patients and their families is mandatory.[35] Palliative care is also a studied subject, and exams in undergraduate medicine throughout the UK have palliative care scenarios and questions in their final exams. Patients should be encouraged to take part and contribute to decisions about their own care and treatment. Care is provided also with consideration to the metabolic state of the patient. This is important when potentially hazardous treatments, which may produce adverse effects, are to be used, i.e. chemotherapy. An improvement in symptoms, decreased rate of progression of cancer, decreased psychological distress for patients and their relatives, and a more peaceful family care were denoted as positive factors in the ideal management of palliative chemotherapy. This is important because although the aim of chemotherapy may not be a cure, there may be patients who still wish to undergo chemotherapy for symptom control to maintain quality of life and others who wish not to receive chemotherapy.[36] Efficacy prediction for treatments in terms of pros and cons and improvement of end-of-life care. An essential and desired aspect for all patients is continuity in care. With an increasing number of cancer patients and a significant number with advanced disease, continued contact with the same healthcare professionals and provision of information is becoming difficult. Patients often have to repeat their history and disease story, and to accumulate knowledge of cancer and its progression is a difficult task. A discussion of forward planning for the patient from the oncologist or general practitioner will enable preferences in end-of-life care to be met. This includes patients who may wish to die at home or others who may wish to remain independently managed within the community. Information on support from Macmillan nurses, Marie Curie nurses, and district nurses should be provided from the result of these discussions to enable patients to apply further support when necessary. Written and recorded information, which may include previous clinic letters and statements of patient preferences, can be useful patient aids. This ideal care will lead into the continuous care provided in the terminal phase and into bereavement with family support by the same or familiar healthcare professionals.[37]

8.2. Symptom Management

For some patients, the symptoms of the cancer or treatment can be difficult to tolerate. At times, increased frequency and urgency can lead to incontinence and a sore bottom. This can be distressing and uncomfortable. There are a number of things that can be done to improve this. Sometimes simply knowing where the nearest lavatory is and being able to access it quickly can be reassuring. Dietary advice with bulking agents and medications can help to slow down the bowel and improve stool consistency. Discuss your problems with your GP or specialist team so that they can help to find the best solution for you. People with incontinence can develop irritation of the surrounding skin. Keeping the skin clean and dry is important to prevent infection.[38] There are barrier creams that can protect the skin and if it has become sore, a mild steroid cream may help. More severe anal discomfort can be caused by hemorrhoids or a split in the back passage (anal fissure). This can cause rectal bleeding and some bright red blood on the toilet tissue. Measures to avoid constipation and straining will help but sometimes these problems require specific treatment and you should discuss this with your doctor. Low red cell levels (anemia) are a common complication of colorectal cancer and can cause fatigue or shortness of breath. This can be improved with blood transfusions for those patients who are fit enough. Finally, cancer is sometimes associated with significant weight loss and loss of appetite. There is no single effective treatment for this but sometimes the use of steroids can improve appetite and a referral to a dietitian can be helpful.[39]

8.3. Emotional Support

Emotional support is also a vital part of dying with dignity. When cancer is advanced and it becomes clear that a cure is beyond medical science, emotional support

can help individuals and families cope with the approaching death in a way that allows for a peaceful and dignified passing.[15]

Psychiatric medication is sometimes necessary when emotions are very intense or when the emotional distress is interfering with medical treatments or the person's ability to take care of himself/herself. Medications can usually be given so that the person can continue to participate in their medical care and interact with their families.[22]

People with cancer and their families may have many emotional needs. Sometimes, the emotional needs are far greater than the physical needs. Emotional support can be provided by healthcare professionals, social workers, mental health counselors, and clergy. Emotional support is also available at support groups and through individual, couple, or family counseling. These services can help people and their families know what to expect and effectively cope with cancer. This is key as effective coping may enhance overall quality of life.[40]

9. Clinical Trials and Research

Colon cancer is a pervasive disease that affects many people across the globe. As the disease becomes more advanced, many patients seek new and different types of treatment when traditional therapies are unsuccessful. Clinical trials are an integral part of that process. These studies test the best new treatment options for cancer and many other diseases. Standard treatment for cancer involves surgery, chemotherapy, and radiation therapy. Some patients go for years only to have their cancer return or their disease become incurable. Others will be treated but current options carry a great risk of side effects. In these cases, clinical trials may offer a new option. In a clinical trial, patients are offered a chance to try the newest treatment options, which could offer more promise and less risk of debilitating side effects. It is important for a patient considering a clinical trial to think about what their current treatment option offers and what could be gained or lost by trying something new. Also, it is important for patients to discuss this with their physician to see if the trials would be a good option for them.[42]

9.1. Importance of Clinical Trials

Clinical trials play a key role in determining whether or not a new treatment is effective. In addition to determining the value of a new treatment, clinical trials can provide valuable information that can be used to improve the quality of life for people with cancer. The most common of the three types of cancer treatment trials, treatment trials test new treatments on people. The main goals of these trials are to find the best treatment for a disease or to improve on the standard treatment. These treatments can vary from medications, surgical procedures, medical devices and can also include alternative and complementary therapies. Clinical trials are the final step in a long process that begins with research in a laboratory. If a treatment proves to be effective in a clinical trial, it may become a new standard of care. Patients with colon cancer should consider enrolling in a clinical trial whenever possible. Keep in mind that even when patients participate in trials, it does not always mean they will benefit from the treatments being studied. They may receive the standard treatment being tested for comparison, which may be the best treatment for their cancer. Sometimes people with cancer feel that the treatments they receive are not the best possible option. Clinical trials give these individuals a chance to contribute to the future of treatment for colon cancer and help improve the quality of life for future patients. By participating in a clinical trial, the patient may have the opportunity to gain access to new treatments that are not yet available to the general public. All in all, clinical trials provide a positive outlook by giving patients hope for a cure or better quality of life and are the best way to prove how effective a treatment really.[43]

9.2. Current Research Studies

As clinical trials and research studies continue to make advancements in methods of preventing, detecting, and treating colorectal cancer, it is becoming more important for a patient to understand their options for treatment. An entire section has been written to describe more about clinical trials, and how a patient can become involved in a trial.[25]

While researchers are testing techniques for preventing colon cancer, they are also examining ways to improve treatment of the disease. An NCI-sponsored trial recently compared the effectiveness of two commonly used surgical techniques for treating colon cancer. The study found that a newer procedure, which creates a temporary opening for waste to leave the body, was better at preserving the patient's quality of life without affecting survival and the chances the cancer would return. This procedure will now be tested in a larger trial to determine if it is superior to the traditional surgery. Other research has focused on improving chemotherapy for patients with more advanced stages of the disease. Studies have been testing new drugs and drug combinations to see if they are more effective in shrinking tumors and extending survival. This includes a study between two different drug combinations to determine which is better in treating patients with advanced colorectal cancer.[44]

Current research studies have focused on developing less invasive techniques that can be used to detect and remove precancerous polyps. Sigmoidoscopy and colonoscopy are methods of detecting polyps. Sigmoidoscopy, a procedure used to look into the rectum and lower colon for polyps, can be used to remove any polyps found during the exam. A colonoscopy is similar to a sigmoidoscopy, but is used to look into the entire colon for polyps. Researchers are comparing the effectiveness of these two methods in detecting polyps. Another technique for finding polyps, which is still being

tested, involves the use of a special camera that takes pictures of the colon. If this is successful, it may eliminate the need for a sigmoidoscopy or colonoscopy. A less invasive way to remove polyps involves the use of a colonoscope with a wire loop. This method has been effective in removing large polyps without the need for major abdominal surgery.[45]

10. Prevention and Lifestyle Changes

Prevention is the key in reducing the incidence of colorectal cancer. The preventive strategies can be put into place at an individual level and for the population as a whole. The preventative strategies can be broken down into those who have been diagnosed with a disease and those that have not been diagnosed with a disease. Secondary prevention is implemented in those people who have already been diagnosed with the disease. This is done through treatment of the disease and the prevention of its spread to other areas of the body. Treatment for colorectal cancer is done primarily through surgery, chemotherapy, and radiation therapy. Surgery has been proven to be the most effective way of preventing the spread of the cancer to other parts of the body. If the cancer is localized or has not spread significantly, surgery is generally the best option. If successful, surgery may be the only treatment required.[44] This type of treatment is what patients should be aiming for as it has considerably fewer side effects than those prevalent with chemotherapy and radiation therapy. If the cancer has spread to other areas of the body, surgery may not be sufficient in prevention of cancer spread. Adjuvant therapy is the term used for the therapy given after local treatment to patients with high risk of developing disseminated disease. Chemotherapy or radiotherapy can be used in an attempt to prevent disease occurring elsewhere in the body.[46]

10.1. Healthy Diet and Exercise

People who eat high-fat diets have an increased risk for developing colon cancer. In 1999, the American Cancer Society published dietary guidelines to help Americans reduce their risk for cancer. Some key factors of the guidelines include: choosing most foods from plant sources, eating five or more servings of fruits and vegetables each day, and eating smaller portions of high-calorie foods. A study conducted by the European Prospective Investigation into Cancer and Nutrition (EPIC) found that consuming large amounts of red and processed meats raises one's risk for colon cancer. Another study has shown that increased levels of fish and omega-3 polyunsaturated fats (fish oil) were linked to a decreased risk of colon cancer. Studies suggest that increased physical activity reduces the risk of colon cancer. Data from the Nurses' Health Study (NHS) showed that increased physical activity after a diagnosis of colon cancer was associated with reduced risk of recurrence and death. The Dietary Intervention in Primary Prevention of Colorectal Cancer (Polyp Prevention Trial) was a major randomized clinical trial designed to test whether a low-fat, high-fiber, high-fruit and vegetable diet could reduce the recurrence of adenomatous polyps – considered to be precursors to colon cancer. After following over 2000 patients in a trial lasting almost 3 years, it was reported that there was no effect on the recurrence of polyps in the intervention group. The negative findings from this trial are believed to be associated with poor adherence to the diet and short duration of the trial. A similar trial conducted with almost 1500 patients, the Women's Health Initiative Dietary Modification Trial, showed that a low-fat diet did not affect the total risk of developing colon cancer, but decreased the risk for obese individuals. Although the positive effects from these trials were minimal and somewhat debatable, they both provide substantial evidence that diet plays a key role in the prevention of colon cancer.[47]

10.2. Smoking and Alcohol Cessation

A new debate is emerging related to the effect of cigarette smoking and the harmful influence of alcohol on the incidence of colon cancer. The increased consumption of high-fat foods that often accompanies smoking and alcohol use is a potential confounding factor in studies on this topic. Although the adverse effects of smoking and heavy alcohol use on gastrointestinal and other cancers are well established, it is not yet clear whether cessation of these practices increases the risk of colon cancer in former smokers and drinkers to the level of people who have never smoked cigarettes or consumed alcohol. An observational study supports an association between long-term smoking and colorectal cancer in postmenopausal women that is stronger for rectal cancer than for colon cancer. Women who quit smoking for 10 years or more had risks similar to those who never smoked, a result suggesting that former smokers can lower their risks by cessation. The increase in colon cancer risk specifically associated with adenomas ranges from 20% to 50%, indicating that it is higher than the 18% increase in risk for small and uncertain lesions seen in the pooled analysis.[48]

10.3. Regular Screening

Screening is a method used to detect the incidence of a disease in individuals who do not yet have symptoms and are undertaken when they are assumed to be at higher than average risk of developing the diseases. The purpose of screening is to identify diseases at an early stage and reduce the incidence of morbidity and mortality. The preferred screening test for colorectal cancer is by colonoscopy, which is usually only undertaken in individuals of moderate to high risk. This is a visual examination of the entire colon and is the most accurate test for colorectal cancer as it can detect lesions as small as 1mm. If this is not possible, other effective methods include flexible sigmoidoscopy, double contrast barium enema, and CT colonography. Although FOBT and immunochemical stool tests are more suitable for population screening due to their lower cost and minimal risk, they are less reliable. If any abnormalities are detected through these tests, then further assessment

and/or referral for colonoscopy is required. Patients with a family history of colorectal cancer are recommended to commence screening at an earlier age, and those who have a personal history of adenomatous polyps, colorectal cancer, or inflammatory bowel disease should undergo periodic surveillance. In cases where the colorectal cancer is due to a hereditary syndrome, surveillance will need to be continued indefinitely. Regular screening can reduce the incidence of colorectal cancer and also detect cancer at an early stage, thus reducing the death rate from the disease.[49]

11. Coping with Colon Cancer

A diagnosis of cancer and the treatment process often has a profound emotional impact on a person. Coping with the changes and challenges of a serious illness can cause a great deal of stress and anxiety, and it may take time for the person to adjust. People with colon cancer and their family members may feel a wide range of emotions including shock, disbelief, denial, anxiety, and fear, as well as a significant amount of emotional pain. This pain may stem from having to confront the possibility of death and from the disruption of lifestyle, self-image, and identity that may result from the cancer and its treatment. Personally coping with a cancer experience involves the ability to tolerate and adapt to changes and the uncertainty that lies ahead, and to keep making decisions that allow one to have hope for the future. Adaptation occurs over time and often people with cancer and their loved ones find that they have good days and bad days, and often the bad days become fewer as time goes on. When first dealing with the burden of colon cancer it is not unusual for a person to feel isolated and alone. Many social activities often become disrupted and sometimes people have a hard time relating to family and friends due to their illness. Despite having a strong network of support many people find that others cannot relate to their situation and often feel uncomfortable talking about the illness. Secondary to this is the reluctance to discuss the illness in order to protect the feelings of family members. While this is sometimes viewed as an attempt to shield loved ones from the stress and pain of illness, in certain situations this reluctance to communicate can create an environment of emotional avoidance. This avoidance often leads to increased feelings of isolation for the patient, and can create a sense of alienation for the primary caregiver. Open communication within the family is essential for maintaining a feeling of togetherness through a difficult time.[50]

11.1. Emotional Impact

Experiencing cancer is an emotional rollercoaster for many patients. Initial reactions to the diagnosis of colon cancer may include denial, anger, fear, and depression. Some patients struggle to deal with the fact that they have cancer. Others may seem to accept the diagnosis yet have much difficulty dealing with the changes that the diagnosis has brought to their lives. Some are able to cope effectively, however, and experience less severe levels of stress. In any case, it helps for individuals to realize that these mood changes are common and to learn ways of coping with their emotions. This may also be helpful for family members and friends in understanding the patient's experience and in dealing with their own emotions. When coming to terms with having cancer, there are a number of emotional concerns that typically arise. Shock upon receiving the diagnosis is common, even if the individual has been feeling very ill. The idea of undergoing treatment and dealing with possible side effects may also cause distress. Patients may become anxious or depressed when left alone to ponder the situation. Some worry about the financial impact of the illness. Cancer can affect the self-esteem as well, since the patient may feel that the changes to their body and lifestyle brought on by the illness lower their dignity. People with colorectal cancer may be troubled by the social stigma of the disease due to its effects on bowel function and incontinence. Throughout the cancer experience, patients and their families may feel that life has become unfair or unjust. These feelings are all normal, but it is important for the patient to address them in a constructive manner.[47]

11.2. Self-Care Strategies

Healthy living strategies that help individuals prevent colon cancer can also assist individuals undergoing treatment for colon cancer. By adopting a lifestyle aimed at prevention, survivors can emerge from treatment stronger, healthier, and feeling more in control of their lives. Those who can't tolerate dietary fiber or don't normally include it in their diet should proceed with caution. It may cause symptoms such as cramping, bloating, or gas, and it should be introduced gradually in small amounts. Dietitians suggest that these symptoms may be due to bacterial fermentation of the fiber, which should decrease over time as the bowel gets used to processing it. Fiber supplements may actually be easier to tolerate than fiber-rich foods since they contain less total fiber. It is essential to maintain good nutrition during and after cancer treatment to optimize recovery. Individuals who are not able to consume adequate food or fluids because treatment has caused nausea, vomiting, diarrhea, or mouth and throat problems may need to modify the type of food they consume to ease these symptoms.[49]

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