

The Research on Recent Cancer Therapies and Their Side Effects

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Abstract. Now the top cause of mortality worldwide, cancer. One in six deaths, or around 10 million deaths, were attributed to it in 2020. Every year, 400000 or so children are given cancer diagnoses. One-third of cancer-related deaths are attributed to factors including smoking, having a high body mass index, drinking alcohol, and not getting enough vitamin C. This study discusses the benefits and drawbacks of the most recent cancer treatments.

Keywords: Cancer Treatment, Physical Surgery, Radiation Therapy, CAR-T Cell Therapy, Side Effects.

1. Introduction

From pre-1890s, the only way to treat cancer is the surgical treatment. Until 1895, the hormonal therapy started to be used to treat breast cancer. After Marie and Pierre Curie found radium in 1900, they started to use radiotherapy. In 1940, the chemotherapy came out, but still had extra hurt on normal cell. By the 1980, targeted therapy started to reduce the extra hurt on normal cells. In 2010, immunotherapy started a new trend of using patients' own immuno system to treat the cancer.

In 2020, new cases of cancer were 19292789 and the Cum. risk was 20.44% for both sexes. The mortality was 9958133 and the Cum. risk was 10.65%. The most common cancer in both sexes was breast cancer (11.7%) and the lung cancer (11.4%). The highest death rate of cancer in both sexes was the lung cancer (18%) and colorectum cancer (11%). Cancer has become the biggest reason of death. Because of the quickly metabolism of the tumor cell and hard to detect in the early state.

CAR-T cell, or chimeric antigen receptor T cells are receptor proteins that have been engineered to give T cells the new ability to target a specific antigen. The receptor are chimeric in that they combine both antigen-binding and T cell activating functions into a single receptor. CAR-T cell therapy is a new type of immunotherapy that use CAR-T cells to treat cancer. The premise of CAR-T immunotherapy is to modify T cells to recognize cancer cells in order to more effectively target and destroy them. It is a latest way of treating cancer. Nowadays, CAR-T cell therapy has been used in treatment of hematological malignancies. It has a significant effect in solid tumor, according to the latest research.

This paper introduces the cancer therapies in common use, about their usage, current limitations and potential strategies. Solid tumors are heterotypic aggregates of many cell types, including cancer cells, cancer stem cells, connective-tissue cells, and immune cells. All of these cells can communicate with one another via specific junctions (tight and gap junction) that maintain and regulate a perfect tumor microenvironment. Several scientific studies have shown that these different genetically designed tumors with acquired resistance could control complex cell-to-cell interactions and aberrant signaling pathways leading to genome instability. Solid tumor can be divided into 3 kinds: malignant, pre-malignant and benign.

Malignant tumors, mainly of monoclonal origin, manifest six essential alterations: growth signals, intensification of anti-growth signals, cell and tissue apoptosis or necrosis, limitless replicative and proliferative potential, prolonged angiogenesis, and organ/tissue invasion followed by metastasis. The tumor's microenvironment interaction with genetics, local nutrient supply, and other organismal factors add further stochasticity. Pre-malignant tumors have strict monitoring that let them have the potential to change into an cancerous tumor. A consequence of the pre-malignant initiation is the production of higher quantities of matrix remodeling proteases and the release of pro-angiogenic,

proliferation, and survival factors within the tumor's microenvironment. Benign tumors are a normal, controlled category of non-cancerous solid tumor that can form anywhere in the body. They have almost the same cellular features as the malignant ones, but they do not have the ability to travel elsewhere in the body to form metastatic sites. Even so, a benign tumor can produce damage if it compresses nearby tissue, vital organs, or blood circulation. In rare cases, such as adenoma or colon polyps, this kind of tumor has the capacity to transition to a malignant state.

2. The therapies had been used to treat cancer

2.1. The physical surgery

The physical surgery is the earliest therapy used by human to treat cancer. With the surgical tools like scalpel and tweezers, doctors will physically remove the cancer cells in patients' body. After several decades, this therapy had developed many different kinds, like robotic surgery and electrosurgery.

2.2. The chemotherapy

Chemotherapy is a drug treatment that uses powerful chemicals to kill fast-growing cells in your body. It is most often used to treat cancer, since cancer cells grow and multiply much more quickly than most cells in the body. Many different chemotherapy drugs are available. Chemotherapy drugs can be used alone or in combination to treat a wide variety of cancers. Though chemotherapy is an effective way to treat many types of cancer, chemotherapy treatment also carries a risk of side effects. Some chemotherapy side effects are mild and treatable, while others can cause serious complications.

The chemotherapy drugs will be given as an infusion into a vein, taken in pill or capsule form, injected with a needle and creams or gels containing drugs. The drugs can be given directly to the cancer, but still have some side effects like nausea, vomiting, diarrhea, damage to lung tissue, heart problems and kidney problems.

2.3. The radiation therapy

Radiation therapy (also called radiotherapy) is a cancer treatment that uses high doses of radiation to kill cancer cells and shrink tumors. At low doses, radiation is used in x-rays to see inside patients' body, as with x-rays of your teeth or broken bones.

External beam radiation therapy comes from a machine that aims radiation at patients' cancer. The machine is large and may be noisy. It does not touch patients, but can move around you, sending radiation to a part of your body from many directions. It is a local treatment, which means it treats a specific part of your body. For example, if you have cancer in your lung, you will have radiation only to your chest, not to your whole body.

Internal radiation therapy is a treatment in which a source of radiation is put inside your body. The radiation source can be solid or liquid. It with a solid source is called brachytherapy. In this type of treatment, seeds, ribbons, or capsules that contain a radiation source are placed in your body, in or near the tumor. Like external beam radiation therapy, brachytherapy is a local treatment and treats only a specific part of your body. With brachytherapy, the radiation source in your body will give off radiation for a while. Internal radiation therapy with a liquid source is called systemic therapy. Systemic means that the treatment travels in the blood to tissues throughout your body, seeking out and killing cancer cells. You receive systemic radiation therapy by swallowing, through a vein via an IV line, or through an injection. With systemic radiation, your body fluids, such as urine, sweat, and saliva, will give off radiation for a while.

Radiation not only kills or slows the growth of cancer cells, it can also affect nearby healthy cells. Damage to healthy cells can cause side effects.

2.4. CAR-T cell Therapy

Chimeric antigen receptor (CAR) T-cell therapy is a way to get immune cells called T cells (a type of white blood cell) to fight cancer by changing them in the lab so they can find and destroy cancer cells. CAR T-cell therapy is also sometimes talked about as a type of cell-based gene therapy, because it involves altering the genes inside T cells to help them attack the cancer.

The immune system recognizes foreign substances in the body by finding proteins called antigens on the surface of those cells. Immune cells called T cells have their own proteins called receptors that attach to foreign antigens and help trigger other parts of the immune system to destroy the foreign substance. The relationship between antigens and immune receptors is like a lock and key. Just as a lock can only be opened with the right key, each foreign antigen has a unique immune receptor that is able to bind to it. Cancer cells also have antigens, but if your immune cells don't have the right receptors, they can't attach to the antigens and help destroy the cancer cells. In CAR T-cell therapies, T cells are taken from the patient's blood and are changed in the lab by adding a gene for a receptor (called a chimeric antigen receptor or CAR), which helps the T cells attach to a specific cancer cell antigen. The CAR T cells are then given back to the patient. Since different cancers have different antigens, each CAR is made for a specific cancer's antigen. For example, in certain kinds of leukemia or lymphoma, the cancer cells have an antigen called CD19. The CAR T-cell therapies to treat these cancers are made to attach to the CD19 antigen and will not work for a cancer that does not have the CD19 antigen.

With around 10 million fatalities, or one in every six, cancer was one of the main causes of death in the globe in 2020. In 2020, there were 2.26 million new cases of breast cancer, 2.21 million new cases of lung cancer, 1.93 million new cases of colon and rectal cancer, and 1.41 million new cases of prostate cancer [1].

The most common malignancies were lung cancer, which claimed 1.80 million lives, followed by colon and rectum, liver, stomach, and colon (all of which claimed 916,000 lives), liver (830,000 lives), and breast cancer (685,000 lives). 400 000 or so children are diagnosed with cancer each year. The most prevalent cancers vary by nation. In 23 nations, cervical cancer is the type that is most prevalent [2].

About one-third of cancer-related deaths are caused by smoking, having a high BMI, drinking alcohol, eating a diet deficient in vitamin C, and not exercising enough. 30% of cancer incidences in low- and lower-middle-income countries are estimated to be caused by conditions including hepatitis and the human papillomavirus (HPV). However, many cancers can be cured if patients receive the proper care and treatment in a timely manner.

In the past 150 years, the cancer therapies have a rapid development. Before 1895, the only way to cure the cancer was the physical surgery. In the early decades, the mortality of cancer surgery was pretty high. After the year of 1895, George Thomas Beatson developed the hormonal therapy, which removed the ovaries and administers thyroid extract in a patient to cure the breast cancer. The next period of cancer treatments is radiotherapy. Thanks to Marie and Pierre Curie found radium, the radiation can be used to treat cancer. The radiation will interact the cancer cell, then break the cancer cell's structure. But at the same time, the radiation may destroy the normal cells beside. The chemotherapy was soon developed because of the fast progressive of pharmacy. The drugs can use the chemicals inside to induce cancer cells' apoptosis. After the development of the monoclonal antibody, the chemotherapy got a new stage called the targeted therapy. The monoclonal antibodies can be directed to specific tumors and molecular alteration. By this way, the damage of the normal cells can be reduced. The next phase of the therapies is the immunotherapy. It uses biological therapies that help the body's immune system fight cancer. Because this therapy uses body's own immune system, the harm to body can be reduced to a new minimum.

A common part of diagnosing and treating cancer is the cancer surgery. Its main purpose is to physically remove cancer. If a patient needs to have a cancer surgery, here are some common reasons might have [3]:

To prevent cancer. For some type of cancer, remove an organ before cancer develops can prevent cancer.

To diagnose. A piece of tissue will be taken in the surgery as a sample. It will be tested in a lab to see if it is cancerous or not. And other tests can check the makeup of the cells. These tests can help to plan the patients' treatment and their health care team to plan what next to do.

To stage the cancer. The surgery will give the clear size of the cancer cell and whether it has spread or not. Through this information can figure out the stage of cancer and tell how serious patient's condition is and if patients need aggressive treatments.

As a primary treatment. For many cancers, surgery is the main treatment.

Surgical debulking. Sometimes the cancer can't be fully removed by surgery. The debulking surgery may remove it as much as possible.

To relieve side effects or symptoms. Surgery can also be used to improve patients' quality of life. For example, it can reduce the pain led by a cancer which oppressing on nerves or bones. If a cancer blocks the intestine, the surgery can remove it too.

Actually, the goal of cancer surgery is to remove all of the cancer from the body as soon as it is possible. In order to do this, cutting tools are used to remove the cancer and some healthy tissue around it. In the surgery, some lymph nodes in the area may be removed. These lymph nodes will be tested to see if any cancer cells are contained in it. If cancer cells spreads to the lymph nodes, the cancer could spread to other parts of the body.

Other types of operations are used to treat cancer. Some other types of cancer surgery are as follows:

Cryosurgery. Very cold material is used in this surgery, like liquid nitrogen spray or a cold probe. These material freezes and destroys cancer cells.

Electrosurgery. This type of surgery uses electric current to destroy cancer cells.

Laser surgery. Beams of light are used to cut off or destroy the cancer cells.

Mohs surgery. This surgery will remove cancer layer by layer. Once a thin layer is removed, it will be studied to look for signs of cancer. This method will repeat until all the cancer is removed. This type of surgery can be used to remove cancers on sensitive parts like skin and eye.

Laparoscopic surgery. Instead of making a single, large incision, this minimally invasive procedure makes multiple, smaller ones. Through the cuts, a tiny camera and surgical instruments are inserted. What the camera observes is displayed on a monitor. This is used by the surgeon to direct the tools used to remove the malignancy. Patients recover more quickly and may experience fewer complications as a result of the smaller incisions.

Robotic surgery. During robotic surgery, the surgeon is situated away from the operating table. A 3D representation of the surgical site is shown to them on a screen. The surgeon uses hand controls to guide a robot that moves surgical instruments to complete the process [4]. The use of robotic surgery enables the surgeon to operate in difficult-to-reach areas. This type of surgery may result in quicker recovery times and fewer complications for the patient.

Natural orifice surgery. Abdominal organs can be operated on without making skin incisions using natural orifice surgery. Instead, medical professionals use a body opening that develops naturally, such the mouth, rectum, or vagina.

Surgery risks vary depending on the kind of procedure the patient is having [5]. The risk of the majority of cancer surgeries is generally:

Pain is a typical aftereffect of most operations. Injuries to more persons than others. The medical personnel will provide patients advice on how to lessen their suffering. They will offer painkillers along with it.

Infection. The medical staff of the patient will instruct them on how to treat their wound following surgery. To prevent infection, adhere to following guidelines. The recuperation period may be prolonged by infections. If patients do get an infection, their doctor may prescribe medications to treat it.

Organ function decline. The doctor might have to remove an entire organ in order to treat the patient's malignancy. For instance, if a patient has kidney cancer, a kidney may need to be removed.

For some of these procedures, the residual organ may function adequately to restore patients' preoperative states of health. In other circumstances, patients could experience certain issues following surgery. For instance, losing a lung might make breathing more difficult.

Patients might not feel particularly energetic after surgery. Patients may experience concentration issues. This is usual, and things will improve.

Bleeding. Bleeding is a possibility with all surgeries. Inform your healthcare practitioner of any medications you are taking. Some medications may make bleeding more likely.

Blood clots. Patients who recently had surgery have an increased chance of getting a blood clot. Despite the low risk, this might be quite serious.

Altered bowel and bladder function. Patients could experience issues urinating or having bowel motions right after surgery. Depending on the patient's operation, this usually improves after a few days.

The radiation therapy is another way of the cancer treatment. Radiation therapy destroys the DNA of cancer cells, which can kill them or, at high dosages, prevent their proliferation [6]. DNA damage that cannot be repaired leads cancer cells to either stop growing or die. After the damaged cells die, the immune system will eliminate and destroy these cells.

Radiation therapy cannot quickly destroy cancer cells. Treatments for several days are essential before the DNA detriment is sufficient to break down the cancer cells. After radiation therapy is finished, these cells will continue to be destroyed for a few weeks or months. Radiation therapy is a treatment option for cancer that can either destroy it, prevent it from returning, or slow its growth.

Palliative therapy refers to methods for relieving symptoms. Tumors may shrink throughout treatment as a result of the external beam radiation, which will help to minimize discomfort and any other side effects the tumor may cause, like breathing problems or bowel and bladder control loss. To relieve cancer pain that has migrated to the bones, a systemic radiation therapy using medications known as radiopharmaceuticals will be administered.

Though, there has some side effects of radiation therapy, like fatigue, hair loss, skin changes and so on [7][8].

The chimeric antigen receptor (CAR)-T cell therapy is an ground-breaking approach in cancer therapy, which has achieved a great success in hematological malignancies and appeared as a prospective treatment manner against solid tumors. It entails extracting T cells from a patient, genetically altering the cells *ex vivo* to let a synthetic receptor to be encoded, which will bind a particular tumor antigens, and then putting the modified cells back into the patients' bodies. The clinical effectiveness of CAR-T cell therapy in treating leukemia and other cancers like it has sparked interest in evaluating the concept in solid tumors. However, compared to haematological malignancies, the biology of solid tumors is more intricate. On the day of June 2, 2021, the phase 1 clinical trial of Tmunity Therapeutics stopped in males with prostate cancer because the immune effector cell-associated neurotoxicity syndrome (ICANS) was blamed to two patients passed away from , which was a setback for CAR-T cell therapy for solid tumors [9].

T cells, as their name implies, are the basis of CAR-T cell therapy because they are responsible for destroying pathogen-infected cells and helping to direct the immune response.

The current CAR-T cell therapies are individualized for each patient. The patient's T cells are used to make their T cells, which are genetically altered to produce CARs on their surface. The CARs attach to cancer cells after identifying specific proteins, or antigens, on their surface. After being "augmented" in the lab to millions of cells, the patient will get the modified T cells. If everything goes as planned, the patient's body will continue to produce CAR-T cells that are able to recognize and destroy any cancer cells that have the target antigen on their surfaces.

However, CAR-T cell treatment still has certain drawbacks. A few examples include antigen escape (the emergence of tumor resistance to CAR designs that target a single antigen), on-target off-tumor effects (solid tumor antigens are frequently also expressed on normal tissues at different levels), and so forth. Some of them could have a variety of negative side effects. such as a high temperature and chills, breathing difficulties, extreme nausea, vomiting, and/or diarrhea, feeling woozy or

lightheaded, headaches, a rapid heartbeat, extreme exhaustion, and/or pain in the muscles or joints [10].

This study shows the cancer death rate nowadays and discussed about the recent days cancer treatments, including physical surgery, radiation therapy and CAR-T cell therapy. The benefits they brought to us and the side effect of them can be more clear by this study. In a long term, cancer treatment will still an important study routine in the medical area. As a difficult point of protecting the health of patients, there will be more therapy being developed and the side effects of these therapies will be reduced as much as possible. For the furthur study, this study can give them a clearer sight of these therapy and their side effect.

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