Current and Future Treatments of Pancreatic Cancer

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Abstract. Pancreatic cancer (PC) is among the most common tumors in the world. Its incidence rate increases with age. More than half of all pancreatic cancer deaths occur in developed regions. The overall prognosis of pancreatic cancer is pretty bad. Only less than 15% of patients can be treated with surgery, and less than 10% of patients are alive after 5 years. The main purpose of the study is to summarize the current and future expectative treatments for pancreatic cancer. To illustrate it more particularly, we also add the basic introduction of pancreatic cancer, including: types of pancreatic cancer, risk factors of pancreatic cancer, symptoms, treatments, new trend, and the problem existing in the modern treatment. Our objective is to let people see and understand the pancreatic cancer clearer and more systematically. The way we study it is by searching information from the internet, picking the most important part, and putting them distinctly. By summarizing the relevant information, the treatments of pancreatic cancer could be improved.

Keywords: Pancreatic cancer, pancreas, therapy, development, drawback.

1. Introduction

The pancreas is a fish-shaped organ that sits behind the stomach, and in adults, it is about 6 inches (15 cm) long but less than 2 inches (5 cm) wide. About 3% of all cancer cases and 7% of all cancer deaths in the US are results of pancreatic cancer, and its incidence rates continue to grow [1]. Pancreatic cancer is the 7th leading cause of cancer deaths worldwide.

Historically, progress in the systemic treatment of individuals with advanced cancer has been slow. However, the progress of treatment over the past 12 years has brought moderate but tangible progress for patients [2]. The foundation of these improvements has been continued development of cytotoxic chemotherapy combinations, including oxaliplatin, irinotecan, Fluorouracil/nanoliposome irinotecan, fluorouracil, folic acid, Gemcitabine plus nab-paclitaxel, and NALIRIFOX [2]. In addition, induction /maintenance has become an option for certain populations (i.e. BRCA or PALB2 mutated patients, whose disease has been stabilized or improved in first-line platinum therapy) to discontinue cytotoxic drugs for a long time. Although this strategy has not yet been widely used and has been proven to increase survival, it provides patients with a less toxic and treatment-free treatment option [2].

At present, according to PRODIGE-4/ACCORD 111 test and MPA, the standard treatment for most patients with metastatic pancreatic adenocarcinoma is permanent cytotoxic chemotherapy using FOLFIRINOX or gicitabine and nanoparticle albumin binding (nab-) paclitaxel [2]. Although both options have been improved compared with the former generation of QIcitabine monotherapy as a first-line treatment, FOLFIRINOX and GIXIPHARMAIN NAB-paclitaxel at no period have been actively compared in forward-clinical trials [2]. However, FOLFIRINOX is usually a first-line treatment for advanced pancreatic cancer, which is well tolerated and approved by the ASCO guidelines, while guiscitabine paclitaxel is retained for second-line or first-line treatment [2]. The recently reported indirect evidence of NALIRIFOX and gemcitabine nab paclitaxel in the recently reported NAPOLI-3 trial further supports this method [2]. In clinical practice, FOLFIRINOX usually modifites its original dose plan, uses a lower dose of IRINOLATEKINE (150 mg/m2 every two weeks), and cancels fluorurin injection to improve adverse reactions while doing no efficacy [2].

By understanding how cancer destroys people's lives and how advances in biology continue to save desperate patients and families, this paper analyzes and discusses in detail the current

development and treatment of pancreatic cancer in the hope that we will be fortunate enough to make some contributions in this regard. This paper will detail the global burden of pancreatic cancer, the different types, risk factors, symptoms, current treatments, shortcomings of current treatments, and new research that can improve the treatment of pancreatic cancer.

2. Main Boby

2.1. Global Burden

About 3% of all cancer cases and 7% of all cancer deaths in the United States are caused by pancreatic cancer (PC), and its incidence rates continue to grow [1]. It's ranked as the seventh ranking cause of cancer death worldwide. The American Cancer Society estimated that the condition of pancreatic cancer in the United States for 2023 is: about 64,050 people, 51.73% of which are male and 48.27% of which are female, will be diagnosed with pancreatic cancer; about 50,550 lives, 52.66% of male's and 47.34% of female's, will be taken away by pancreatic cancer. Hence, we can conclude that pancreatic cancer is slightly more widespread in male than in female. More than half of all PC deaths occur in developed regions.

2.2. Types

Pancreatic cancer comes in several forms. Types of exocrine cancer that are less prevalent, pancreatic adenocarcinoma, and ampullary cancer are all types of pancreatic cancer [1]. The most commonly seen cancer of the pancreas is pancreatic duct adenocarcinoma (PDAC) accounting for over 90% of cancers [3]. Distinguishing which type of pancreatic cancer, a patient has is very important for both patients and their doctors. Unique treatments should be given according to different conditions.

2.3. Risk Factors

There are many risk factors of pancreatic cancer and here we classify them into two types: risk factors that are changeable and risk factors that are unchangeable [1]. First is tobacco use. One of the most significant contributors to risk for pancreatic cancer is smoking. People who smoke have approximately twice the risk of developing pancreatic cancer as those who have never smoked [4]. It's believed that tobacco use might have induced around one quarter of all pancreatic cancers over the world. The use of smokeless tobacco products and cigarette smoking also increase the risk. Fortunately, it seems that the influence of smoking begins to dwindle when smoking is given up. The second is being overweight. Being very overweight, or obese, is a contributor to pancreatic cancer. Obese individuals, that is, those with a body mass index (BMI) of at least 30, have an additional 20% chance of suffering from pancreatic cancer. Growing weight as an adult could add additional risk as well. Even for people who are not too overweight, excessive weight around the waist is also a risk factor. Third is chronic pancreatitis. When the inflammation reaction maintains for a long time, it might indicate a higher risk of having PC. Chronic pancreatitis, a continued inflammation of the pancreas, is related to an increased risk of pancreatic cancer. Drinking alcohol and smoking might cause chronic pancreatitis. Fourth is access to some chemicals in workplace. When people keep in contact with certain chemicals at work, especially in the metal processing and dry-cleaning professions, their risk of getting pancreatic cancer may be increased [5]. Fifth is diabetes. People with diabetes are more likely to get pancreatic cancer. The specific mechanism for this is still to be studied. While whether type 1 diabetes have a higher risk for people is not clear, it's clear that type 2 diabetes is the most closely related risk with pancreatic in all diabetes. Type 2 diabetes is becoming more common in young people while the average weight of this group of people also tend to rise. People of higher age groups having this type of diabetes might be accompanied with obesity.

The factors above are those that can be changed, and the following are those that are hard to change. Older people tend to have a higher risk of getting pancreatic cancer. Almost all patients with pancreatic cancer are older than 45. About 67% of patients are at least 65 years old. In average, the

patients are typically diagnosed around 70 years old. Males have a slightly higher possibility of developing pancreatic cancer than females. However, it's not clear yet whether the higher risk in men is due to the greater rate of people who smoke.

The risk of pancreatic cancer is slightly less for whites than African Americans. The reasons for this are still to be studied, but it's speculated that it might is because that more African Americans have diabetes, smoke, and have a higher weight. Pancreatic cancer appears to be related to inheritance. An inherited syndrome may be responsible for the high risk in certain families. The gene leading to the increased risk is not known within other families.

2.4. Symptoms

Unfortunately, it's hard for doctors to diagnose pancreatic cancer through finding any indications. Symptoms usually appear only until the tumor starts having an impact on other organs of the digestive system. Hence, over 80% of the cases of pancreatic cancer are discovered and treated at later stages, which is usually too late for appropriate surgeries. Here are some symptoms of pancreatic cancer.

Jaundice means yellowing of the skin or the eyes. It could also be caused by bruises, medication, and excessive drinking of alcohol. Bilirubin is a dark brown pigment contained in the bile. Bile is produced by the liver and exists in the bile duct, a tube connecting the liver and pancreas. However, pancreatic cancer can block the bile duct, making the bilirubin accumulating. This buildup of bilirubin will be reflected on the skin as a yellow of color. Dark urine (pee), light colored stool (poop) and itchy skin could also be caused by this process.

Silent jaundice is a classic symptom, but abdominal pain is more commonly presented in between 60 percent and 80 percent of patients [7]. Pancreatic obstruction in more advanced cases can cause symptoms of pancreatic collapse, such as post-prandial abdominal pain and steatorrhea [8]. Moreover, patients may suffer from venous stasis again and again, which causes splenomegaly with portal or splenic vein compression [9]. Regrettably, these findings are discovered in the later stage of the disease, which means they are facing more advanced cases along with worse results [8]. Upper abdomen and back pain, exhaustion, flatulence, inappetence, thrombus, weight decrease, and feelings of disgust are all signs indicating you may have pancreatic cancer [6].

2.5. Treatments

Some of the treatments for patients presently are: immunotherapy, targeted therapies, drugs targeting immune system checkpoints, radiation therapy, surgery, vaccines for cancer, individualization of therapy, anti-angiogenesis factors, chemotherapy, growth factor inhibitors, and monoclonal antibodies.

Screening for pancreatic cancer is not recommended to asymptomatic average-risk people. The incidence of developing pancreatic cancer of individuals during their lifetime is only 1.6%. Previous documents have also shown that no suitable means for early pancreatic cancer screening have been developed. Though some projects have been trying to use standardized screening methods, the primary method used for screening is still endoscopic ultrasonography (EUS). Lucas et al.'s estimation is that even with a hypothetical screening instrument with 99% sensitivity and 99% precision (which is actually nearly impossible to reach), 1000 healthy individuals will be incorrectly diagnosed with PC when the experiment is done on 100,000 individuals [10]. Additionally, the harms of screening for pancreatic cancer may include: pain caused by the examination, adverse events related to anesthesia, and mental stress or anxiety. According to current standardizations, only if the healthy individuals have a risk of developing PC equal to or greater than 5% that they should be given with screening [11].

2.6. Problems

Although there are some treatments that can respite pancreatic cancer, there are still some problems posted here. A research team has used a piece of testing equipment that can analyze nutrients in blood [12]. They assessed the ability of around 20 different human pancreatic cancer cell lines to absorb

more than 175 nutrients without glucose [12]. They found that uridine is a fuel for cancer cells [12]. In addition, they also found a close relationship between the hyperactivity of a gene named UPP1 and the use of uridine by pancreatic cancer cells. The latter discovery is an important part of this puzzle [12]. The specific details have not been proofed yet. The biggest problem of pancreatic cancer is that they have few effective treatments, and it is quite noticeable whether there are possibilities to find new therapies [12]. Even though there are finding about cancer cell metabolism, there's still a lot of work to be done to find a way to use it for feasible treatment [12]. There is also a potential treatment called KRAS-Targeted Drug, which has shown possibilities against pancreatic cancer [13]. The Dr. Stanger has emphasized that the next important step for it is using them in people to assure the treatment has enough safety [13]. Things are still not finished yet, and it might face several problems in the future. Also, research has shown that abnormal collagen might be the pancreatic cancer's weak spot [14]. But there is still lots of works to do if they want to understand how widespread collagen is [14]. From the above examples, it can be seen that even if there are some breakthroughs in the treatment of pancreatic cancer, they can be explained by theory, but it is still difficult to get a clear treatment for the final pancreatic cancer. Because at present, there are some high-possible breakthroughs in the research, many of which cannot be explained by scientists, and it is also difficult and may take a lot of time from theory to practical clinical treatment. Pancreatic cancer is still a big problem waiting for people to solve.

2.7. Improvements Of Cytotoxic Chemotherapy

Recently approved, combined with 5-Fluorouracil, leucovorin and liposomal irinotecan can be used for metastatic pancreatic cancer after the progression of the treatment gemcitabine-based rigimen based on the worldwide, randomized phase III NAPOLI-1 trial [2]. Clinically, this alliance has always been confined to the 2nd-line or 3rd-line settings of those with progressive diseases who are still waiting for treatment [2]. In the phase I/II study, the combination of NALIRIFOX (liposomal irinotecan 50 mg/m2, Fluorouracil 2400 mg/m2, leucovorin 400 mg/m2 and oxaliplatin 60 mg/m2) was valued on the first and 15th days of the 28-day cycle and proved controllable toxicity and a median total survival rate of 12.6 months, which generated preparatory data for determining the quality of this combination in phase III trials [2].

3. Conclusion

About 3% of all cancer cases and 7% of all cancer deaths in the United States are caused by pancreatic cancer. It ranks as the 7th leading cause of cancer death worldwide. More than half of pancreatic cancer deaths occur in developed regions. One of the most significant contributors to risk for pancreatic cancer is smoking. Unique treatments should be given according to different conditions. Being severely overweight (obesity) is the number one risk factor for pancreatic cancer. People who are obese, that is, body mass index (BMI) of 30 or above, have an additional 20% chance of suffering from pancreatic cancer. Growing weight in adulthood also increases the risk. The third is chronic pancreatitis, which is continued inflammation of the pancreas. The fourth is access to some chemicals in workplace.

Unfortunately, it's hard for doctors to diagnose pancreatic cancer through finding any indications. Symptoms usually appear only until the tumor begins to affect other organs in the digestive system. Pancreatic cancer appears to be related to inheritance. An inherited syndrome may be responsible for the high risk in certain families. The gene leading to the increased risk is not known within other families. The biggest problem of pancreatic cancer is that they have few effective treatments. Even though there are findings about cancer cell metabolism, there's still a lot of work to be done to find a way to use it for potential treatment. There are also developments in the treatment of pancreatic cancer such as the combination of 5-Fluorouracil, leucovorin, and liposomal irinotecan recently approved for metastatic pancreatic cancer. Through this passage, readers could have a more thorough comprehension of pancreatic cancer. This passage could play a role in disseminating and

documenting research results. However, the problems listed above is not given with corresponding solutions. The unceasing development of studies related to pancreatic will be the way forwards.

Authors Contribution

All the authors contributed equally and their names were listed in alphabetical order.

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