

Different therapies in pancreatic cancer treatment

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Abstract. Pancreatic cancer is a devastating disease, which is characterized by high mortality, mainly due to advanced diagnosis and limited treatment options. Recent research has made great progress in dealing with this challenge. This has led to progress in all aspects of pancreatic cancer management, including improved screening strategies, the implementation of new assisted therapy, enhanced the results of surgical results, surgical technology, the development of more effective chemotherapy plans, optimization of radiation treatment solutions, and exploration of targeted treatments and targeting a single genetic characteristic. In addition, the continuous survey of immunotherapy may change the treatment method. However, there is still a significant gap in knowledge, especially when identifying reliable biomarkers to detect and prognosis prediction in the early stage, the customization of individual patients' treatment plans and the unique microenvironment that overcomes pancreatic tumors. Despite these challenges, the continuous development landscape of pancreatic cancer has brought hope to patients and emphasizes the importance of continuing research work to improve the quality of life of people who are struggling with such powerful diseases.

Keywords: Pancreatic cancer, subtypes, therapies, targeted therapy, immunotherapy.

1. Introduction

Pancreatic cancer is indeed devastating, not only suitable for people but also for their families. This is a particularly fatal form of cancer. Its survival rate is frustrating, mainly because it is usually diagnosed at the advanced stage and the treatment plan is limited. In fact, this is the fourth main reason related to cancer, not only in the United States but also in other countries. This emphasizes that people urgently need to deepen their understanding of disease, enhance early testing methods and formulate more effective treatment strategies.

The pancreas is an important organ, which plays a dual effect in digestion and endocrine systems. The outer secretion of the pancreas will secrete digestive enzymes released in the small intestine. These enzymes help the disintegration of carbohydrates, protein and fat in the foods, thereby promoting nutritional absorption. The endocrine part of the pancreas, especially the islets of Langerhans, produces hormones such as insulin and pancreatic hyperglycemia. These hormones regulate blood glucose levels to ensure that the human body maintains proper glucose balance.

There are many subtypes in pancreatic cancer. Pancreatic adenocarcinoma (PDAC) is the most common type of pancreatic cancer, accounting for about 85 % to 90 % of all cases. PDAC starts with the pipeline of the pancreas, and these pipelines bring digestive enzymes to the small intestine. It is known for its aggressive behavior and post-diagnosis [1]. Pancreatic adenocyte cell carcinoma is a rare

and distinct form of pancreatic cancer that originates from the glandular structures responsible for producing pancreatic enzymes. It stands out from the more common pancreatic ductal adenocarcinoma (PDAC) with its unique clinical presentation and treatment approaches. Pancreatic colloid cancer, another uncommon subtype of exocrine pancreatic cancer, is characterized by the presence of mucinous materials within tumor cells. Compared to PDAC, it often carries a more favorable prognosis, offering hope for better treatment outcomes. In contrast, pancreatic cystoma primarily affects children and is exceptionally rare among adults. It arises from undeveloped pancreatic cells and tends to exhibit a more positive outlook in pediatric cases. These diverse forms of pancreatic cancer underscore the complexity of the disease and the need for tailored approaches to diagnosis and treatment.

Endocrine pancreatic cancer, also known as pancreatic neuroendocrine tumors (PNETs), can be categorized into two main types: functional and non-functional PNETs [2]. Functional PNETs are capable of producing hormones, leading to a range of hormone-related symptoms. These tumors can be further classified based on the specific hormones they generate, such as insulin-producing tumors causing low blood sugar, gastric tumors producing digestive enzymes, glucose-producing tumors leading to high blood glucose levels, and growth-inhibitory tumors affecting growth-regulating hormones. In contrast, non-functional PNETs do not produce hormones, often remaining asymptomatic until they reach a more advanced stage or metastasize to other organs. Diagnosing non-functional PNETs may be challenging, and treatment can be more complex due to their typically later-stage detection.

It is important to note that the differences between these subtypes usually require special tests, including tissue pathological analysis and chemical staining of immunohistochemical tissue to accurately identify the type of pancreatic cancer of patients. The choice of treatment and prognosis may change significantly, depending on the specific subtype.

Several factors can heighten the risk of developing pancreatic cancer. Age is an important factor, and most cases occur in individuals 65 and over. A family history of pancreatic cancer or certain genetic mutations can also increase risk. Smoking is a recognized risk factor, and being overweight or obesity will increase the possibility of developing this cancer. In addition, the long-term inflammation (referred to as pancreatitis) of the pancreas is related to an increased risk of pancreatic cancer. These risk factors jointly promote the prevalence and incidence of this disease.

Pancreatic cancer presents several formidable challenges that contribute to its high mortality rates. One major issue is the delayed diagnosis, as pancreatic cancer is often asymptomatic in its early stages, leading to detection only after it has already spread, reducing the feasibility of effective treatment plans. Additionally, pancreatic cancer is known for its aggressive growth and rapid spread, making it difficult to control. Surgical intervention is a primary treatment method, but not all patients are eligible due to the advanced stage of the disease or their overall health status. Furthermore, pancreatic cancer cells can develop resistance to chemotherapy and radiation therapy, diminishing the effectiveness of these treatment modalities. Unlike some other cancers, there is no widely accepted screening method for early detection among the general population, further complicating the diagnosis and treatment process. Consequently, the overall 5-year survival rate for pancreatic cancer remains relatively low, typically around 10% or less, primarily due to the challenges associated with advanced diagnosis and limited treatment options [3]. This article summarizes the different treatment methods and research of pancreatic cancer in recent years, in order to provide a reference for future exploration of more effective treatment methods.

2. Therapies on pancreatic cancer

Screening is a valuable tool not only for detecting early-stage pancreatic cancer (PC) but also for finding signs of potential trouble, like intraductal papillary mucinous neoplasm (IPMN) [4] and pancreatic intraepithelial neoplasia (PanIN). Screening mainly focuses on people at high risk, and these high-risk people can be divided into two groups: those with inherited risks and those without. The non-inherited risks include factors like being over 55, smoking, obesity, excessive alcohol use, diabetes, certain diets, exposure to harmful substances, and long-term pancreas inflammation (chronic pancreatitis). On the other hand, the inherited risks involve conditions such as , familial adenomatous polyposis (FAP),

familial pancreatic cancer (FPC), Peutz-Jeghers syndrome, and familial atypical multiple mole melanoma (FAM).

2.1. Neoadjuvant therapy

Neoadjuvant therapy, which is treatment given before surgery, has shown promising benefits in localized pancreatic cancer (LPC). Studies have shown that it can improve the possibility of successful resection of tumor (R0 split), reducing the opportunity to return cancer in nearby regions, and help to identify patients who may not benefit from surgery. Immediately after local disease surgery, auxiliary therapy can receive some form of treatment through neo-assisted therapy, even if it has the risk of delaying potential healing surgery. Neo-assisted chemotherapy involves a combination of a separate chemotherapy or a 5-FU or Gascotabita chemotherapy [5], and it may include chemotherapy before surgery. Its survival rate is equivalent to the survival rate of surgery before the treatment. Although the risk of surgical complications is slightly higher, the therapy of neo-assisted therapy subsequent surgery is considered more cost-effective. Postoperative complications and mortality are similar to LPC surgery that immediately surgery. Neo-assisted therapy provides a reasonable replacement method for the traditional “surgical advantages” method for LPC treatment.

2.2. Surgery

Surgery plays a crucial role in the treatment of pancreatic cancer, particularly for patients with resectable tumors. The primary surgical procedure used is pancreatoduodenectomy, widely known as the Whipple procedure. During this surgery, surgeon removed the head of the pancreas, the duodenum and the bile duct and the stomach. Then connect the rest of the pancreas to the digestive system. For localized and resectable pancreatic cancer, surgery provides the best opportunity for long-term survival. Patients diagnosed at an early stage when the tumor is confined to the pancreas can undergo curative surgery with the intent to remove the entire tumor. However, it is crucial to accurately determine resectability before surgery to avoid unnecessary procedures and complications.

2.3. Chemical therapy

Chemical therapy plays a key role in the treatment of pancreatic cancer. It is not only a major treatment method but also an auxiliary therapy after surgery. The treatment strategy involves drugs designed to stop cancer cell growth or induce them to destroy them. The chemotherapy scheme for pancreatic cancer usually combines a combination of drugs. If it is categorized as removable marginality, neoadjuvant chemotherapy is often performed before surgery, the purpose is to reduce tumor size and promote surgical resection. In this case, drugs that are usually used in chemotherapy include the combinations of Nab-Paclitaxel and Folfirinox [6], Fluorouracil, Leucovorin, Irinotecan, Oxaliplatin [7]. After surgery, auxiliary chemotherapy may open a prescription due to hindering the recurrence of cancer. In this case, 5-fluorouracil (5-FU) is one of the frequent drugs. In addition, chemotherapy is usually the main treatment method for patients with local advanced or metastatic pancreatic cancer. Compared with single-drug therapy, combination therapy (such as Folfirinox and Gemcitabine binding NAB-chain metamamide) shows higher survival and response rates. Nevertheless, chemotherapy may bring various challenges, including disgust, fatigue, hair loss, and bone marrow suppression. The effective management of these side effects to ensures that patients can continue to use the treatment plan while retaining their quality of life.

2.4. Radiation therapy

Radiation therapy is an important part of many ways to treat pancreatic cancer, involving precise use of high-energy beams to target and eliminate cancer cells. This method can be used as part of the comprehensive pancreatic cancer treatment plan combined with surgery and chemotherapy. Preoperative radiation therapy conducted strategic treatment in certain cases before surgery to reduce the tumor, thereby improving the feasibility of surgery, especially the patients with removable tumors. After surgery, it is called auxiliary radiation therapy. Auxiliary radiation therapy was used after surgery to eliminate

any remaining cancer cells and reduce the risk of local recurrence. In addition, palliative radiation therapy plays a vital role in improving the quality of life quality of patients with advanced pancreatic cancer that cannot be removed through surgical resection, because it effectively manages painful symptoms such as pain and obstructive jaundice. However, it is necessary to acknowledge the challenges related to radiation therapy, including potential side effects such as fatigue, skin irritation and digestive problems. Strict planning and diligent monitoring are important to minimize these adverse reactions. At the same time, optimize the treatment benefits of radiation therapy, and emphasize its importance in pancreatic cancer management.

3. Targeted therapy and Immunotherapy

Nursing standards for patients with pancreatic tube adenocarcinoma (PDAC) are focused on chemical treatment plans and pancreatic cancer surgery. However, limited treatment methods, advanced tumor phase of advanced diagnosis, and PDAC aggression help to help the high mortality rate. In recent years, many measures have begun to transform novel scientific discoveries into forward-looking clinical trials. One of the main ways to pursue the hierarchy of PDAC patients according to the tumor transcription group to predict the treatment reaction. Other strategies are concentrated in genomic changes and the identification of personalized targeting therapies. Further experimental studies are conducting new biomarkers for testing for cancer diagnosis, subtypes, treatment reactions prediction or clinical results. However, the challenge is still to transfer knowledge to clinical practice.

The research of targeted therapies has been devoted to identifying specific subgroups of pancreatic ductal adenocarcinoma (PDAC) patients based on their molecular characteristics, with the aim of tailoring targeted therapies to their individual genetic profiles. Recent breakthroughs have highlighted the effectiveness of maintenance PARP inhibition in treating PDAC tumors that carry harmful mutations in genes like BRCA1, BRCA2, and PALB2 [8]. Furthermore, the long-standing challenge of targeting the KRAS gene, a common mutation in PDAC, has seen promising developments with the emergence of KRAS G12C inhibitors [9], offering hope for next-generation KRAS-focused therapies in PDAC. As more precision-targeted therapies continue to be developed, the era of precision medicine holds the potential to profoundly transform the treatment landscape for patients with metastatic PDAC.

Immunotherapy has always been a changer in rules for cancer treatment and uses the human body's own immune system to fight cancer cells. However, due to the unique characteristics of the pancreatic microenvironment, its application in pancreatic cancer is particularly challenging. In the clinical trials of pancreatic cancer, examination point inhibitors such as Pembrolizumab and Nivolumab have been studied, which aim to block proteins that hinder immune cells attacking cancer cells [10]. However, the results were mixed, and only some patients responded to immunotherapy positively. In order to improve the effectiveness of immunotherapy, researchers are exploring joint therapy. These therapies match immunotherapy with other therapies (such as chemotherapy and targeted therapy) to enhance the immune response to pancreatic cancer. The immunosuppressive nature of overcoming pancreatic tumors is still a major challenge for immunotherapy. The focus of research is to determine predictive biomarkers and formulate strategies to solve these obstacles. At the same time, with the study of emerging therapy and innovative methods, the field of pancreatic cancer treatment continues to develop, and it is expected to improve the results in the future.

4. Conclusion

In the realm of pancreatic cancer treatment, remarkable progress has been made in recent years, offering a glimmer of hope to patients grappling with one of the deadliest malignancies. In short, the landscape of pancreatic cancer treatment is developing rapidly. The progress of surgery, chemotherapy, radiation therapy, targeted therapy and immunotherapy provides new hopes for patients who face such devastating diseases. However, it is necessary to recognize the remaining challenges and complexity of pancreatic cancer. It provides hope in the future direction of research and treatment, but the consistent efforts of researchers and decision-makers need to overcome obstacles and improve the prognosis of pancreatic

cancer. As the journey of effective pancreatic cancer continues, perseverance to save lives and improve the quality of life of people who fight with such powerful enemies.

References

- [1] Zhou, B, Xu, J W, Cheng et al 2017 Early detection of pancreatic cancer: Where are we now and where are we going? *Int J Cancer* 1412 231-241
- [2] Lee, D W, Kim, M K, & Kim, H G 2017 Diagnosis of pancreatic neuroendocrine tumors *Clin endoscopy* 506 537-545
- [3] Kleeff J, Korc M, Apte M, La Vecchia C et al 2016 Pancreatic cancer *Nat rev Dis primers* 21 1-22
- [4] György L, Gábor B, Fiore, Net al 2006 Pancreatic intraepithelial neoplasia PanIN and intraductal papillary mucinous neoplasms IPMN. *Magyar Sebeszet* 591 12-19
- [5] Khawaja M R, Kleyman S, Yu Z et al 2017. Adjuvant gemcitabine and gemcitabine-based chemoradiotherapy versus gemcitabine alone after pancreatic cancer resection: the Indiana University experience. *Am J Clin Oncol-canc* 401 42-46
- [6] Chiorean E G, Cheung W Y, Giordano G, et al 2019 Real-world comparative effectiveness of nab-paclitaxel plus gemcitabine versus FOLFIRINOX in advanced pancreatic cancer: a systematic review. *Ther Adv Med Oncol* 11 1758835919850367
- [7] Park H S, Kang B, Chon H J et al 2021 Liposomal irinotecan plus fluorouracil/leucovorin versus FOLFIRINOX as the second-line chemotherapy for patients with metastatic pancreatic cancer: a multicenter retrospective study of the Korean Cancer Study Group KCSG esmo open 62 100049
- [8] Voutsadakis, I. A., & Digkila, A. 2023 The Landscape and Therapeutic Targeting of BRCA1, BRCA2 and Other DNA Damage Response Genes in Pancreatic Cancer *Curr Issues Mol Biol* 453 2105-2120
- [9] Bannoura S F, Khan H Y, & Azmi A S 2022 KRAS G12D targeted therapies for pancreatic cancer: Has the fortress been conquered? *Front Oncol* 12 1013902
- [10] Yu Q, Tang X, Zhao W et al 2021 Mild hyperthermia promotes immune checkpoint blockade-based immunotherapy against metastatic pancreatic cancer using size-adjustable nanoparticles *Acta Biomaterialia* 133 244-256