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Application and Research Status of ^{125}I Seeds Brachytherapy in Unresectable Pancreatic Cancer

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Abstract: Pancreatic cancer is a digestive system tumor with high degree of malignancy. At present, systemic chemotherapy is the main treatment method. However, due to the difficulty in early diagnosis and easy spread of pancreatic cancer, the survival cycle of patients is short and the treatment effect is poor. ^{125}I seed brachytherapy has obvious advantages in the treatment of malignant tumors, and has been widely used in the treatment of unresectable pancreatic cancer. Either used alone or combined with chemotherapy, the treatment of ^{125}I seed brachytherapy can effectively relieve pain, improve life quality and prolong survival. However, there are few reports about the application status. This article reviews the current updates of ^{125}I seed brachytherapy for resectable pancreatic cancer, and expounds the application status of ^{125}I seeds brachytherapy in combination with monotherapy chemotherapy, dual drug chemotherapy, targeted therapy, immunity therapy, palliative surgery, external radiotherapy and traditional Chinese medicine. Based on the retrospective review, future directions of research and development of brachytherapy for unresectable pancreatic cancer is also proposed, to provide better treatment care for pancreatic cancer patients. At present, there are still many problems to be solved, such as formulating the principles and standards for the application of radioactive particle implantation in the comprehensive treatment of pancreatic cancer; We will continue to standardize and optimize the operation process and distribution means of radioactive seed implantation technology, and better promote 125I radioactive seed implantation technology.

Keywords: ^{125}I Seeds, Brachytherapy, Advanced Pancreatic Cancer, Combination Therapy, Chemotherapy

1. Introduction

Pancreatic cancer is the sixth leading cause of cancer death in China, and is one of the most aggressive and deadly human cancers, characterized by early local invasion and distant metastasis [1]. Despite advances in the diagnosis and treatment of pancreatic cancer, the 5-year survival rate for pancreatic cancer has changed little over the past few decades, consistently below 10 percent [2]. Currently, the only possible cure for pancreatic cancer is radical surgery [3] Unfortunately, 80% of patients with metastatic or locally advanced pancreatic cancer at the time of initial diagnosis have already missed the best time for radical surgery, and the median survival time is only 4 months [4]. Pancreatic cancer responds poorly to surgical resection or chemotherapy, and chemotherapy alone or combined with chemotherapy is the main treatment regardless of whether surgery is performed [5].

In recent years, ^{125}I Particle brachytherapy (^{125}I-ibt, alone or in combination with other therapies, is widely used to treat inoperable cancers, ^{125}I-ibt maximizes the radiation dose of the tumor while reducing radiation damage to surrounding normal tissues, thereby significantly inhibiting local invasion and prolonging overall survival [6].^{125}I-ibt has attracted a lot of attention because of its unique advantages, such as its ability to deliver a tumor-targeted dose of radiation into the tumor during a single operation, and its ability to reduce external radiation exposure and kill the tumor for weeks or months [7, 8].^{125}I-ibt has been considered as a promising

treatment for unresectable pancreatic cancer, so this review reviews its use alone or in combination with chemotherapy, targeted therapy, immunization, palliative surgery, external radiotherapy and traditional Chinese medicine in the treatment of unresectable pancreatic cancer.

2. ^{125}I Particle Brachytherapy

Radioactive particles implantation is a kind of close radiotherapy, the radioactive particles directly inserted into tumor tissue or cancer infiltration tissue graft, sound use of radioactive elements of gamma rays, and direct effects on tumor cell DNA molecule chain, kill phase in DNA synthesis and mitosis of tumor cells, so as to achieve the effect of treatment of tumor [9]. Currently, the commonly used radioactive particles are ^{125}I particle, ^{192}Ir particles and ^{103}Pd particles. It should be noted that particles suitable for brACHYtherapy need to have a certain ability to penetrate human tissue, which can kill tumor tissue to achieve the therapeutic effect, while avoiding damage to surrounding normal tissue [10]. In addition, an appropriate half-life is also required. Lazarescu et al. believed that after radioactive particle implantation, the decrease rate of tumor cell killing was equal to the rate of tumor growth for a period of time, and the effective time of treatment was related to the doubling time of tumor cells. Therefore, the length of radioactive particle half-life was closely related to the curative effect [11]. ^{125}I particle release the low-energy gamma rays, has a half-life of 59.7 days, can penetrate tissue distance of 1.7 cm, for pancreatic cancer cell proliferation and rapid, can be targeted killing and avoid damage the surrounding normal tissues, as well as through direct action to tumor of retroperitoneal tumors to ease and splanchnic nerve plexus invasion and oppression, obviously relieve pain, Improve patients' quality of life [12]. Therefore, partial center application ^{125}I particle is undergoing brachytherapy for pancreatic cancer. However, compared to conventional external radiation therapy, ^{125}I After all, particle implantation is an invasive operation, which may lead to adverse reactions such as bleeding, pancreatic fistula and biliary fistula. Caution should be paid to the occurrence of these adverse reactions when using particle implantation for treatment.

CT guided ^{125}I Patients with particle implantation underwent abdominal CT scan before surgery to determine the specific location, size and shape of the tumor. After that, THE CT image was imported into the TPS treatment system for 3D reconstruction, to delineate the tumor target area and organs at risk, determine the number of needles and particles, and draw the isodose curve. Patients are generally placed in supine position, and appropriate puncture sites and puncture routes are selected after CT scan positioning, followed by TPS plan under real-time CT guidance ^{125}I. During the operation, attention should be paid to the protection of peripheral large vessels and important organs. CT should be reexamined immediately after the operation and introduced into the TPS treatment system to observe the distribution of particles and check the number of particles, and evaluate the implementation of the plan. If there is an obvious dose deficiency area, namely the cold area, replantation can be carried out [13-16]. Multiple center studies showed cT-guided radioactivity ^{125}I Particle implantation in unresectable pancreatic cancer has a significant short-term efficacy, which can effectively control tumor cell growth, reduce tumor volume, relieve pain and improve quality of life. Chen C et al. retrospectively analyzed 42 patients with locally advanced pancreatic cancer with obstructive jaundice. All patients underwent percutaneous biliary stent implantation, and the treatment group received CT-guided implantation ^{125}The results showed that the median OS of the treatment group was 11.67 months, while that of the control group was 9.40 months. The effective rate (complete remission + partial remission) of the treatment group was 72.7%, while that of the control group was only 30% at 6 months follow-up, and no serious complications occurred in all patients [14]. Li Hongwei et al. observed 90 cases ^{125}I No serious complications occurred in the pancreatic cancer patients after particle implantation, including 31 cases with complete remission of cancer pain, 17 cases with partial remission, and 14 cases with ineffective treatment. The median survival time was 11±0.7 months, and the reexamination 2 months after the operation showed that the treatment effective rate was 61.6%, including 7 cases with complete remission and 48 cases with partial remission [15]. Liu Ying et al. observed 90 cases ^{125}I Patients with pancreatic cancer after particle implantation showed significant improvement in spirit, sleep and pain relief. The effective rate of treatment was 61.6% 3 months after operation, including complete remission in 11 cases and partial remission in 26 cases [16].

The other way ^{125}I Particle implantation Ultrasound-guided percutaneous puncture is also being carried out in many centers in China ^{125}I Particle implantation, ultrasound-guided percutaneous transgastric wall ^{125}I Particle implantation and laparoscopic ultrasound guidance ^{125}I. Particle implantation and laparotomy guided by ultrasound ^{125}I Studies on particle implantation. Du Siyun et al. observed 53 cases of ultrasound-guided percutaneous puncture ^{125}I After particle implantation, the incidence of adverse reactions was 18.87%, and all patients were relieved after treatment. In this study, the rate of pain relief was 90.0% and the response rate was 73.6% 3 months after surgery, including complete remission in 17 cases and partial remission in 22 cases [17]. Fu Ping et al. observed 65 cases of ultrasonics guided percutaneous puncture through gastric wall implantation ^{125}I None of the patients with advanced pancreatic cancer treated with radioactive particles had serious adverse reactions, and the pain relief rate was 90.38%. The effective rate 3 months after surgery was 80%, including 19 cases of complete remission and 33 cases of partial remission [18].

It follows that, ^{125}I The efficacy of particle implantation in the treatment of unresectable pancreatic cancer is certain, and the particle implantation of different technologies has been proved to be a safe and effective treatment method, which

has obvious effects on tumor control, pain relief and improvement of patients' quality of life. But only a few studies have provided data on the survival of pancreatic cancer patients who received particle implants, ^{125}I Whether particle implantation as a local treatment can control the local tumor progression and prolong the survival time of patients still needs further research.

3. ^{125}I Particle Brachytherapy + Chemotherapy

Studies by Balaban et al. confirmed the basic role of chemotherapy in the treatment of advanced pancreatic cancer, but chemotherapy alone was poor in the control of pancreatic cancer and could not effectively prolong the survival of patients [19]. At present, the main treatment for advanced pancreatic cancer is concurrent chemoradiotherapy, which inhibits the growth of tumor cells by chemical drugs and kills abnormal cells in patients, thus controlling the development of the disease and achieving therapeutic effect. For advanced pancreatic cancer patients, combined chemoradiotherapy can play a relatively ideal effect [20]. But, as a retroperitoneal organ pancreas, adjacent to the more important blood vessels and organs, the deep location, traditional radiation in the treatment of poor precision and tumor dose is insufficient, the inefficiency of traditional radiotherapy of tumor control, and the particle implantation can effectively solve the problem of insufficient dosage, try to be the most conformal radiation therapy, the tumor control effect is more ideal [21].

Gemcitabine has been widely used in the systemic treatment of locally advanced and metastatic pancreatic cancer, according to the NCCN guidelines. Gemcitabine, as a pyrimidine nucleotide analogue, is an anti-metabolic anticancer drug that acts on the DNA synthesis stage of tumor cells and inhibits the DNA synthesis of tumor cells by interfering with DNA synthesis and repair of tumor cells, thus leading to tumor cell apoptosis [22]. In addition, gemcitabine has radiotherapy synergistic effect in combination ^{125}I Particle implantation and gemcitabine treatment significantly improve the outcome of pancreatic cancer treatment. Zhong Zhenwu et al. observed 40 patients with pancreatic cancer, 20 of whom underwent laparoscopy ^{125}I Particle implantation combined with gemcitabine chemotherapy, 20 patients only received gemcitabine chemotherapy, abdominal pain relief rate of the combined group was 80%, the abdominal pain relief rate of the chemotherapy group was 50%, the incidence of adverse reactions between the two groups showed no statistical difference [23].

Particle implantation + gemcitabine + cisplatin combined with cisplatin chemotherapy in pancreatic cancer has a higher rate of disease control and progression-free survival than gemcitabine alone [24]. Cisplatin is a heavy metal complex, which can act on purine and pyrimidine bases of DNA of tumor cells, inhibit the DNA replication process of tumor cells, and has a strong broad-spectrum anticancer effect [25]. Luo M et al. retrospectively analyzed 66 patients with stage III and IV pancreatic cancer, 35 of whom underwent CT-guided treatment ^{125}I Particle implantation combined with GP (gemcitabine + cisplatin) chemotherapy, 31 patients received only GP chemotherapy. The pain relief and abdominal distension control in the combined group were significantly better than that in the chemotherapy group, and the objective remission rate was 71.4% in the combined group and 41.2% in the chemotherapy group 3 months after the operation. There was no statistical difference in the adverse reactions between the two groups. Median progression-free survival was 7.00±0.30 months in the combination group and 5.00±0.75 months in the chemotherapy group, but there was no statistical difference in median survival between the two groups [13]. Holliway et al. observed 30 patients with pancreatic cancer under CT guidance ^{125}I particle implantation, the postoperative combined use of GP (gemcitabine plus cisplatin) scheme chemotherapy, postoperative 1 month review shows treatment effective rate was 63.3%, complete response in 3 cases, partial in 16 cases, postoperative 3 months review shows treatment effective rate was 50.0%, including complete remission in 2 cases, partial in 13 cases, no serious adverse reaction occurred postoperatively [21]. Fu Yujuan et al. observed 86 patients with intermediate and advanced pancreatic cancer, and 43 patients were only guided by CT ^{125}I Particle implantation, 43 patients underwent particle implantation combined with GP (gemcitabine + cisplatin) chemotherapy, the objective response rate of the particle implantation group was 23.26%, and that of the combined group was 34.88%, and the quality of life of the combined group was higher than that of the particle implantation group [26]. Huang Siqi et al. observed 143 patients with advanced pancreatic cancer and 72 patients underwent CT guidance ^{125}I Particle implantation combined with GP (gemcitabine + cisplatin) chemotherapy, 71 patients received only GP chemotherapy, and the pain relief rate was 80.6% in the combined group and 40.1% in the chemotherapy group. The median survival time was 12.5 months in the combined group and 10.1 months in the chemotherapy group. There was no statistical difference in adverse reactions between the two groups and the remission rate of jaundice in the combined group was significantly better than that in the chemotherapy group [22].

Gemcitabine is an anti-tumor drug that inhibits DNA synthesis. The median survival time of patients with advanced pancreatic cancer who received gemcitabine in combination with chemotherapy with diagotene was 10.1 months [27]. Tegafur is an oral fluorouracil anti-tumor drug, consisting of tegafur, gemacil and otiracaspotassium. Tegafur is metabolized into 5-FU in the liver in vivo, which plays an anti-tumor role. Gemacil can slow down 5-FU metabolism, increase the concentration of 5-FU in the tumor, and enhance the anti-tumor effect. Otilaxik can reduce the gastrointestinal toxicity of 5-FU without affecting the antitumor effect [28]. In addition, gemcitabine increased the activity of 5-FU, which in turn enhanced the antitumor effect of diagio [29].

Based on gemcitabine, the combined use of Ticio capsule can reduce the toxicity and side effects, and oral administration is easier, which can not only reduce infusion injury, but also improve the treatment compliance of patients [30]. Gemcitabine 1000mg/m is currently widely used in the treatment of advanced pancreatic cancer in China 2 Days 1 and 8 were administered with tio 40mg/m^2, 2 times a day, oral administration, day 1 to 14, every 21 days for a cycle. Multiple studies have shown that for patients with advanced pancreatic cancer, combined use of particle implantation brachytherapy and gemcitabine and gonow double medicine chemotherapy can make significant benefit patients, patients' objective response rate (complete response rate + partial remission rate), a significant rise in the pure chemotherapy group, and no statistical differences in adverse reactions. Xingguang Chen et al. observed 212 patients with pancreatic cancer and 106 patients underwent ultrason-guided percutaneous treatment ^{125}I Particle implantation combined with GS (gemcitabine + tigio) regimen chemotherapy, 106 patients only received GS regimen chemotherapy, and the objective response rate of the combined group was 91.51%, while that of the chemotherapy group was 75.47%. There was no statistical difference in adverse reactions between the two groups, indicating that in ^{125}I Particle implantation combined with GS chemotherapy can effectively improve the efficacy without increasing adverse reactions [31]. Heanli et al. observed 83 patients with intermediate and advanced pancreatic cancer, and 37 patients were guided by CT^{125}I The objective remission rate of the combined group was 52.78%, and that of the chemotherapy group was 29.79%. There was no statistical difference in adverse reactions between the two groups. Comparing the long-term efficacy, PFS of the combined group was 10.7 months. PFS of the chemotherapy group was 6.1 months, median OS of the combination group was 13.2 months, and median OS of the chemotherapy group was 9.8 months. The efficacy of the combination group was significantly better than that of the chemotherapy group [32]. Shi Guangyong et al. observed 82 patients with advanced pancreatic cancer, and 41 patients were guided by CT^{125}I Particle implantation combined with GS (gemcitabine + tegio) regimen chemotherapy. 41 patients received only GS chemotherapy, and the objective remission rate was 29.27% in the combination group and 4.88% in the chemotherapy group, and the combination group had obvious advantages in relieving pain [33].

Gemcitabine combined with albumin-bound paclitaxel showed greater benefit than gemcitabine alone in patients with advanced pancreatic cancer [34]. The median survival time of patients with advanced pancreatic cancer treated with gemcitabine and albumin-bound paclitaxel was 8.5 months [35]. Albumin-bound paclitaxel uses nanoparticles of albumin as the carrier to improve the efficacy of paclitaxel and reduce the adverse reactions of paclitaxel. Paclitaxel acts on tumor cells during mitosis, inhibits the proliferation and division of tumor cells, thus playing an anti-tumor role. Huang Feilong et al. compared with laparoscopy alone ^{125}I In patients with advanced pancreatic cancer treated with particle implantation brachytherapy and combined treatment with albumin-bound paclitaxel and gemcitabine chemotherapy, the 1-month response rate was 48% in the particle implantation group and only 16% in the combined chemotherapy group [36].

In conclusion, the efficacy of brachytherapy with particle implantation is significantly better than that of the combined chemotherapy group, but whether particle implantation can be combined with gemcitabine combined with albumin-bound paclitaxel chemotherapy remains unknown, and patient survival data is not provided. At present, there are few studies on particle implantation combined with gemcitabine and albumin-bound paclitaxel dual-drug chemotherapy, and no articles have been published, requiring further research.

4. ^{125}I Particle Brachytherapy + Targeted Therapy

At present, non-surgical treatment of pancreatic cancer is still dominated by chemotherapy, but the survival of patients with advanced pancreatic cancer is limited by either chemotherapy. Some progress has also been made in the application of targeted therapy in the treatment of pancreatic cancer. Epidermal growth factor receptor (EGFR) inhibitors, tyrosine kinase receptor (TKI) inhibitors, insulin-like growth factor inhibitors, VEGF receptor inhibitors and ALK inhibitors have achieved certain efficacy in the treatment of advanced pancreatic cancer. However, there are no clear reports that targeted therapy can significantly benefit patients with pancreatic cancer. Erlotinib combined with gemcitabine has been shown to significantly prolong survival [37] Erlotinib is currently the only targeted drug in the NCCN guidelines. Although many targeted drugs have not been proved to significantly prolong the survival of patients with advanced pancreatic cancer, they can be used as radiotherapy sensitizers and have a good application prospect in advanced pancreatic cancer. EGFR inhibitors, Transforming growth factor-β (TGF-β) inhibitors and heat shock protein (HPS) 90 inhibitors can be used as radiosensitizers for pancreatic cancer. EGFR inhibitors can alter cell cycle distribution and inhibit DNA damage repair by inducing apoptosis, blocking proliferation and accelerating regrowth induced by radiotherapy [38-41]. Nituzumab can block the binding of EGFR to its ligand, and has anti-angiogenesis, anti-cell proliferation and pro-apoptotic effects on egFR-overexpressed tumors. Gao C et al. confirmed in vitro cell experiments that ntuzumab can enhance the sensitivity of pancreatic cancer cells to radiotherapy and chemotherapy by enhancing cell cycle arrest and apoptosis [42]. However, whether nituzumab can and ^{125}I The combined application of brachytherapy with particle implantation has not been reported in relevant literature. TGF-β inhibitors can increase the sensitivity of cells to radiotherapy by regulating ATM, BRCA and Rad 51 [43-45]. HPS90 inhibitors have a significant radiosensitization effect on a limited range of

epithelial cancer types [46, 47]. Mitogen-activated proliferation kinases (MAPK) and protein kinase B(Akt) are potential targets for radiotherapy sensitization of pancreatic cancer, which need further study [48]. However, ^{125}I The clinical studies of particle implantation brachytherapy combined with targeted therapy for unresectable pancreatic cancer are rare, which deserves the attention of pancreatic cancer researchers.

5. ^{125}I Particle Brachytherapy Plus Immune Checkpoint Inhibitor Therapy

In recent years, immunotherapy has become the treatment method of emerging malignant tumors. Studies have shown that immunotherapy combined with other therapies has a significant therapeutic effect on a variety of malignant tumors [49]. However, immunotherapy did not show any significant effect in the treatment of pancreatic cancer [50, 51]. This is because pancreatic cancer is resistant to primary immune checkpoint inhibitor treatment. Pancreatic cancer cells change their phenotype by activating pancreatic stellate cells to become myofibroblasts, and then produce a large number of extracellular matrix proteins, resulting in dense fibrotic matrix around tumor cells, and dense stromal cells can prevent CD8+Tumor infiltrating lymphocytes enter tumor tissue and produce strong immunosuppression [52, 53]. Some studies have shown that radiotherapy can promote the release of tumor antigens to stimulate the immune response to attack tumor cells, and radiotherapy may improve the sensitivity of immunotherapy [54].^{125}I It has not been confirmed that whether particle implantation brachytherapy combined with immunotherapy can benefit patients with advanced pancreatic cancer, which is one of the directions that can be explored in the treatment of advanced pancreatic cancer.

6. ^{125}I Particle Brachytherapy + Palliative Surgery

Patients with advanced pancreatic cancer have missed the best opportunity for radical surgery, but palliative surgery combined with brachytherapy can prolong survival for patients with advanced pancreatic cancer. Huang Hongjun et al. reported a combination of palliative surgery in patients with advanced pancreatic cancer ^{125}I The efficacy, pain relief rate and clinical response rate of particle implantation were 71.4%, and the longest known survival was 22.5 months, which is still being followed up [55]. Due to the lack of relevant studies reported in recent years and the small sample size of huang Hongjun et al. 's study, the combination of palliative surgery cannot be concluded ^{125}I The conclusion that particle implantation brachytherapy benefits patients with advanced pancreatic cancer, which needs more research to support.

7. ^{125}I Particle Brachytherapy + External Radiotherapy

Three-dimensional conformal radiotherapy has been widely used in patients with unresectable advanced pancreatic cancer. But always study confirmed that pancreatic cancer is not sensitive to radiation therapy, this is because there are rich in fiber matrix pancreatic cancer, these fiber matrix as a physical barrier to limit tumour cell toxin infiltration, and produce hypoxic microenvironment, reduce the radiotherapy curative effect, but there are also studies confirm close joint external radiation therapy, radiation therapy of pancreatic cancer local control has good effect, Can improve local control rates and reduce complications, possibly because their combination can reduce the dose of 3D conformal radiotherapy and compensate for implantation ^{125}I The dose "cold spot" produced by particle radiotherapy, thus ensuring the uniformity of the total radiotherapy dose rate and radiotherapy dose distribution, and also reducing the dose exposure to surrounding normal tissues [56, 57]. Li Xiaoqin et al. observed 27 patients with advanced pancreatic cancer, 21 of whom underwent intraoperative ultrasound guidance ^{125}I Particle implantation brachytherapy, 3d conformal radiotherapy 5000cGy/28 times and gemcitabine chemotherapy. 19 patients completed the combination therapy, among which 12 patients had a survival time of more than 12 months, with a median survival time of 10.1 months and a total effective rate of 79.85% [58]. Although chemotherapy is the main systemic therapy for advanced pancreatic cancer, radiotherapy is rarely used, but this is a promising research direction. The combination of internal and external radiotherapy can achieve effective dose without damaging surrounding normal tissues.

8. ^{125}I Particle Brachytherapy + Traditional Chinese Medicine

In recent years, Traditional Chinese medicine has also played a role in the treatment of pancreatic cancer. Wang Jiangwei et al. believe that Traditional Chinese medicine, as an adjunctive therapy, has proved to have a synergistic effect when combined with multiple treatment methods in the treatment of pancreatic cancer [59]. Guan Zi et al. believed that Traditional Chinese medicine preparations could play a better role in the microenvironment of pancreatic cancer and had certain advantages [60]. However, there is no relevant study on the combined application of brachytherapy with particle implantation and Traditional Chinese medicine, and further research is needed.

9. Outlook and Summary

In conclusion, pancreatic cancer has insidious onset and difficult diagnosis. Most patients with pancreatic cancer have missed the best opportunity for radical surgery when they are found. Moreover, because of the deep position of the

pancreas, it is difficult to give effective dose without damaging normal tissues, and there is a physical barrier of fiber matrix, which is not sensitive to radiotherapy. The current treatment is based on chemotherapy and systemic therapy. Due to the ^{125}I particles can be directly implanted into the tumor tissue, effectively solving the problem that the tumor location is too deep, and giving effective dose to the cancer tissue while avoiding damage to the surrounding important blood vessels and organs. ^{125}I Brachytherapy with particle implantation has become one of the effective methods for palliative reduction and improvement of quality of life for patients with advanced pancreatic cancer. It can effectively relieve pain alone or in combination with systemic chemotherapy, with significant clinical efficacy. However, its combined application with external radiotherapy, targeted therapy, immunotherapy, palliative surgery and Traditional Chinese medicine therapy still needs further research.

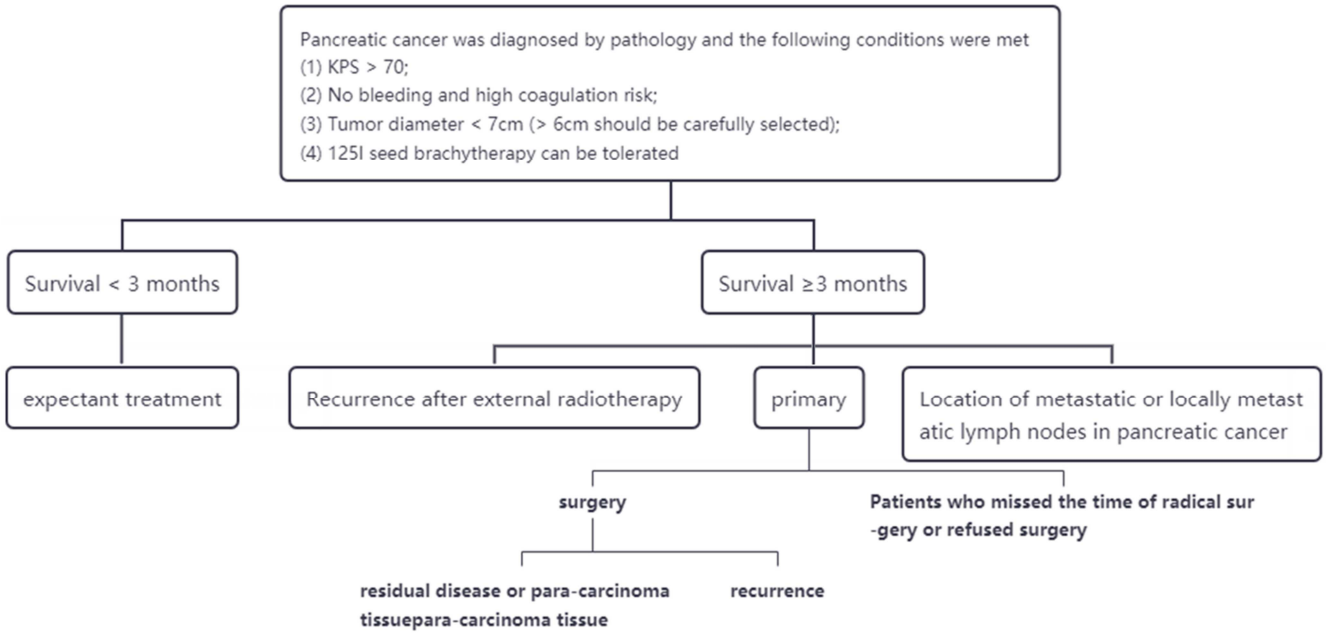

Figure 1. *Treatment options.*

It is expected that gemcitabine and other chemotherapy drugs and targeted drugs such as nituzumab can increase the sensitivity of pancreatic cancer tissue to radiotherapy, which can be further increased ^{125}I The efficacy of brachytherapy with particle implantation, and for emerging immunotherapy in recent years, radiotherapy may improve the sensitivity of immunotherapy. This conclusion needs more studies to confirm. ^{125}I The combination of brachytherapy with particle implantation and targeted drugs and immunodrugs is superior to traditional therapy, and further research is needed. In the future, ^{125}I Particle implantation brachytherapy combined with targeted therapy and immunotherapy may further benefit patients with advanced pancreatic cancer.

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