PERSPECTIVES

# Pancreatic Cancer: Current Situation and Challenges

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Pancreatic cancer, which is characterized as an occult disease, has a high degree of malignancy, and ductal adenocarcinoma accounts for more than 90% of pancreatic cancer. It is accompanied by delayed diagnosis, low resection rate, high mortality rate, and poor prognosis. In recent years, the incidence of pancreatic cancer is on the rise. Because the diagnosis is mostly late, only 10–20% of the patients can be arranged for surgical treatment according to the imaging examination. The 5-year survival rate of patients with pancreatic cancer is only 10–25%. The survival rate of the patients with lymph node metastasis is even lower. It is estimated that by 2030, pancreatic cancer will become the second most common cause of cancer-related mortality in human beings, while the lung cancer will still remain at the top spot in the list[1].

The incidence and mortality rates of pancreatic cancer are increasing, but the progress of therapy development still remains stagnant and the treatments do not seem to be able to grapple with the rising prevalence of pancreatic cancer cases in a commensurate manner. Such a phenomenon will soon become a major public health problem threatening human life and health. The root cause of this alarming challenge can be traced to the minimal effect of the three-level preventive measures that are used to control and treat pancreatic cancer.

1. Primary prevention (etiology-based prevention)

It is difficult to treat pancreatic cancer, but preventive measures may be able to reduce the risk factors. However, the exact etiology of pancreatic cancer is currently not clear. Smoking, obesity, diabetes, alcoholism, and family history are the only high-risk factors that have been identified so far. Smoking causes 30% of the pancreatic cancer cases, and other known high-risk factors collectively account for 10%. Of note, risk factors were not known in 50% of the pancreatic cancer cases[2]. The pathogenesis of pancreatic cancer is unknown. Nonetheless, many hypotheses about its pathogenesis have been proposed, which pointed to gene mutation as the basis of pathogenesis of pancreatic cancer. Mounting evidence also showed that the occurrence of tumor is the result of unpredictable mutations coupled with the alterations in the environmental factors. Given the complexities in the etiologies and pathogenesis of pancreatic cancer, it is highly difficult to prevent the development of pancreatic cancer using the etiology-based approach.

2. Secondary prevention (early diagnosis)

The early diagnosis rate of pancreatic cancer is only about 5%. This is because the general cancer screening methods, such as the use of tumor markers and ultrasound, have proved to be of little significance in the early diagnosis of pancreatic cancer[3]. Most doctors used computed tomography, endoscopic ultrasonography (EUS), EUS-guided fine-needle biopsy, and endoscopic retrograde cholangiopancreatography

(ERCP) to screen the high-risk population of pancreatic cancer, and found that EUS and ERCP had high sensitivity and specificity for detecting pancreatic cancer, but they are unable to meet the clinical needs for early diagnosis of pancreatic cancer[4,5]. The early diagnosis of pancreatic cancer is of great significance and is the key to improve survival. Since the natural course of pancreatic cancer is more than 20 years, theoretically, early diagnosis of the cancer is possible. However, effective screening method that allows early diagnosis of pancreatic cancer is hitherto unavailable. This would put a burden on the health-care resources allocated for the treatment of pancreatic cancer, especially when many of the patients who require the treatment are already in advanced stage.

3. Tertiary prevention (clinical treatment)

Surgical resection is the only treatment option for pancreatic cancer, and radical resection is particularly important. However, surgery is not associated with good therapeutic effect. With only 30–50% of $R_0$ resection cases that have been confirmed by pathology, the resection is accompanied by 80% of local recurrence rate within 2 years and only 20–30% of 5-year survival rate. The effect of surgery on pancreatic cancer was not satisfactory[6,7]. Despite the progress of chemotherapy drugs, the improvement of drug delivery methods, and the rapid development of radiotherapy technology, the treatment of pancreatic cancer still remains ineffective. The main problems in this regard are cancer recurrence, metastasis, and complications. Therefore, the application of independently administered surgery, radiotherapy, or chemotherapy is difficult to achieve a good therapeutic outcome. Instead, a more comprehensive treatment would be able to effectively treat the advanced pancreatic cancer.

Pancreatic cancer is an invasive disease and most of the patients are associated with local tumor progression or metastasis. Further studies on unraveling the molecular targets and pharmacogenomics of pancreatic cancer will provide an insight for developing more effective treatment methods which are personalized and tailored to the needs of each pancreatic cancer patient. The potential biomarkers that can be used as molecular targets for diagnosis and treatments include transforming growth factor-β[8], phospho-glycogen synthase kinase-3[9], phosphoglycerate kinase 1[10], and ubiquitin-specific protease 22[11]. Although the clinical research in pancreatic cancer is still in its most challenging phase in which more promising results are still pending, at present, molecular cloning, gene chip, human genome project, immunotherapy theory, and modern molecular biology techniques have laid a solid foundation for the in-depth study of pancreatic cancer[12,13]. The application

of molecular approaches stands a promising chance to clearly illuminate the occurrence and development of pancreatic cancer and to enable the rapid discovery of new targets for diagnosis and treatment.

With the advent of global networking, digital information, nanotechnology, and other cutting-edge technologies, it is our belief that the crossover of different disciplines with each other will result in the synthesis of new theories, methods, technologies, and equipment which would give us a clearer picture of the pathogenesis of pancreatic cancer and ways to treat the cancer or impede its progression.

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## Conflicts of interest

The authors declare no conflicts of interest.

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