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Review

An Overview of Pancreatic Cancer Diagnosis and Treatment in China: Current Landscape and Future Prospects.

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Abstract

This comprehensive literature review is to summarize the most recent findings regarding the causes, diagnosis, and treatments of pancreatic cancer and to encourage additional investigation into this under-researched malignant tumor. Pancreatic cancer is a significant public health issue in China, with annual mortality rates almost equal to incidence rates. The disease is more prevalent in rural areas and has a poor prognosis. The data was collected from the following databases: Pub Med, Cross ref, Science Direct, Scopus, and Google Scholar we reviewed published articles from 2018 to 2023 on the annual incidence of pancreatic cancer in China is 5.1%, with only 5-7% of patients completely cured. The prognosis is extremely poor, with a 1-year survival rate of 8% and a 5-year survival rate of 3%. Pancreatic cancer has no specific clinical manifestations or tumor markers, and its characteristics are not typical of high-risk factors including smoking, alcohol, chronic pancreatitis, abnormal microorganism metabolism, blood type, and glucose and lipid levels. For increased detection and survival rates, pancreatic cancer must be diagnosed as early as possible. However, the low specificity of tumor markers calls for more study. Future treatment strategies could include immunotherapy and a microbiology-free system, and it's anticipated that they'll offer intriguing clinical applications for extending patients' lives with pancreatic cancer. Finally, we suggest measures to improve the health outcomes of pancreatic cancer patients in China.

Keywords: Pancreatic Cancer; Tumor Markers; Immunotherapy; Diagnosis; Treatment.

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Introduction

Pancreatic cancer (PC) has become more common over the past several years. It contributes to 5% of cancer-related deaths and around 2% of all cancers. Most patients have no overt symptoms until the disease progresses to advanced pancreatic metastasis when tumor cells are very invasive. It has become one of the most fatal malignant tumors, and early diagnosis is challenging [1]. Pancreatic cancer represents a substantial public health challenge in China, where its incidence and mortality rates rival those of malignant tumors. This alarming trend underscores the severity of the disease and its significant impact on the population's health. With a high incidence rate, a considerable number of new cases are diagnosed annually, placing a burden on healthcare resources, and necessitating urgent attention from policymakers and healthcare providers. Furthermore, the mortality rate associated with pancreatic cancer is equally concerning, indicating the dire need for improved prevention, early detection, and treatment strategies to mitigate its devastating effects on individuals and families across the country. In the UK, it accounts for 5.6% and 5.3% of cancer-related deaths, ranking fifth. China's rapid urbanization, lifestyle changes, and aging environment have led to a 9% increase in pancreatic cancer-related deaths in the past decade. Despite improvements in diagnosis and treatment, the survival rate remains below 8%, making it a major issue faced by medical circles both domestically and internationally [2]. Advancements in pancreatic cancer diagnosis and treatment have improved accuracy and sensitivity, with new diagnostic modalities like MRI scanners becoming routine in high-volume centers. Chemotherapeutic agents like gemcitabine and 5-fluorouracil are moderately effective but not significant in terms of survival. A prospective study in China collected medical records, pathological reports, and imaging reports for subject eligibility evaluation [3]. However, at present, there are no standard programs in the world to screen patients with a high risk of PC. To improve the prognosis of pancreatic cancer patients, we reviewed recent advances in risk factors, diagnosis, and treatment of PC.

Risk Factors

Risk factors for PC include non-modifiable factors like age, sex, blood group, family history, genetic susceptibility, diabetes, and modifiable factors like intestinal microflora, smoking, alcohol, chronic pancreatitis, obesity, dietary factors, and infection.

Non-Modifiable Risk Factors

Age

It is highly rare for young persons under 30 to have PC; the disease usually affects older folks. 90% of newly diagnosed individuals are older than 55, with the majority being in their 70s and 80s [4].

Sex

Pancreatic cancer (PC) incidence is lower in women globally, particularly in developed countries. Steroid levels in women may protect against PC. Menopausal hormone therapy (MHT) can reduce PC prevalence by 23%, 35%, and 60% compared to non-administered MHT, with 1-2 years being more effective [5].

Epidemiology of China

China is the largest developing country and faces increasing urbanization, aging, and environmental pollution, leading to a shift in the disease spectrum from infectious to non-infectious diseases, including pancreatic cancer, which has increased rapidly despite lower incidences in Western countries [6].

Area

PC incidence varies globally, with African Americans having higher rates in the US and Asian Americans and Pacific Islanders having the lowest. In China, the cancer burden is increasing due to socioeconomic differences [7].

Challenges and Future Direction

Worldwide, more than 330000 patients are diagnosed with pancreatic cancer every year, and survival rates have barely changed over the past 40 years. In China, both the prevalence and mortality of pancreatic cancer are rising. In 2035, approximately 77497 men and 52868 women in China will be diagnosed with pancreatic cancer, according to a recent forecast from GLOBOCAN (2012). Up till then, over 130000 individuals per year die from pancreatic cancer [8]. According to the prognosis, pancreatic cancer incidence and death in China may rise more quickly in the upcoming years, and the country will have to deal with a significant pancreatic cancer burden [Fig1]. Pancreatic cancer multidisciplinary teams are scarce in China's centers, highlighting the urgent need for effective management. The Chinese government should invest in research, education, and healthcare to improve care quality and reduce morbidity and mortality. Expanding cancer registries and recognizing shortfalls in funding can also help improve national statistics.

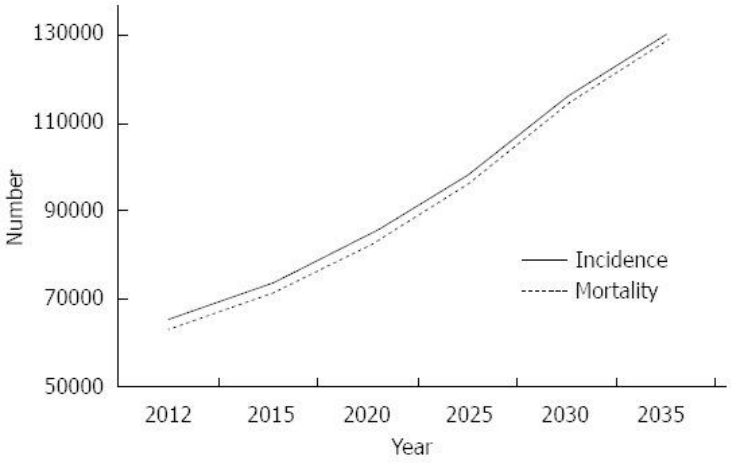

Fig 1 Estimated pancreatic cancer incidence and mortality in the next 20 years in China according to Globocan 2012.

Status treatment of pancreatic cancer

Screening for early Pancreatic Cancer develops over a long time, with an average of 17 years from cancer-initiating cells to metastatic cancer subclones, followed by death after 2.7 years. A screening program for high-risk individuals can improve outcomes. However, there is no nationwide screening program in China due to insufficient data, equipment, and insurance coverage [Fig2]. High-risk individuals in China may be older than 40, have a family history of pancreatic cancer, have new-onset diabetes, have chronic pancreatitis, or have heavy tobacco or alcohol use [9].

Histological Examination

The "gold standard" for the diagnosis of PC is histopathologic evaluation and/or cytology. All patients, apart from those undergoing surgical resection, should work toward obtaining a precise pathological diagnosis before developing a therapeutic strategy. The following procedures are now used to collect specimens for cytology and histopathology: (1) Endoscopic ultrasonography (EUS) or CT-guided biopsy: (2) cytology of ascitic fluid (3) Diagnostic laparoscopy or open surgery with exploratory biopsy.

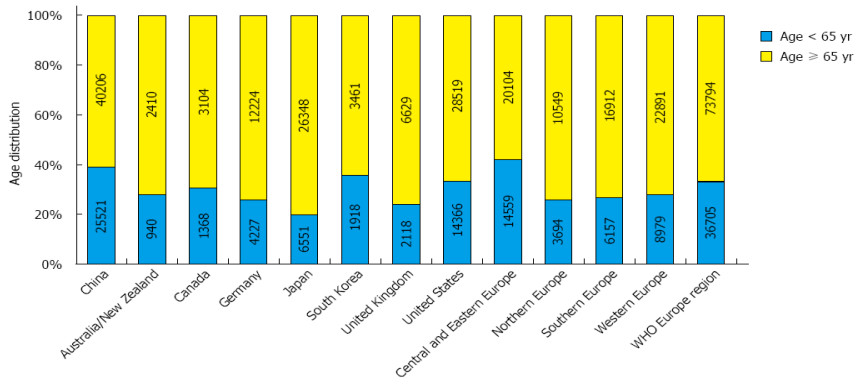

Fig 2: Comparison of the mortality-to-prevalence ratio of pancreatic cancer between China and some major countries and continents.

Tumor Biomarkers

Our understanding of Pancreatic ductal adenocarcinoma molecular alterations has considerably expanded in recent years, and this has made it possible to find new serum tumor indicators. CA19-9, CA242, carcinoembryonic antigen (CEA), CA125, microRNAs, and K-RAS gene alterations are the six most prevalent tumor biomarkers now in PC [10].

Combining tumor markers and imaging methods may be the best choice for early PC screening, with studies showing increased sensitivity and specificity with CA19-9 and CA125, and potentially more diagnostic than separate detection [11].

Advances in cytology and genomics have led to the use of microRNAs and CA19-9 for early diagnosis of prostate cancer. CA19-9 is the most used indicator for postoperative detection in PC recurrence and prognosis. Circulating cell-free DNA (CfDNA) and mutation-specific circulating cell-free tumor DNA (CftDNA) have been identified as potential biomarkers for evaluating cancer efficacy and estimating tumor volume [12].

Fig 3: Overview of biomarkers in pancreatic cancer

Biomarkers	Sensitivity (%)	specificity (%)
CEA	45	75
Carcinoembryonic antigen-related cell adhesion molecule-1	85	98
ca 19-9	80	73
Span-1	81-94	75
DUPAN-2	48-80	75-85
Macropage inhibitory cytokine1	90	62

Alpha4GnT	76	83
PAM4	77	95
Pancreatic juiceDNA methylation	82	100
Fecal K-ras	77	81

Circulating tumor DNA

Circulating tumor DNA (ctDNA) was first detected in tumor patients' serum of cancer patients in 1977 and in pancreatic cancer patients in 1983. It mainly comes from necrotic, apoptotic, CTC, and exosomes. CtDNA contains gene information for tumor cell mutations, aiding in tumor diagnosis and individual medication guidance [13].

Computed Tomography/Positron Emission Tomography

Multidetector computed tomography (MDCT) is a routine examination for diagnosing suspected pancreatic lesions, assessing resectability, assessing vascular invasion, and diagnosing metastatic disease. MDCT can display small branch vessels, peripancreatic vessels, and vascular anatomical variations, allowing for a better understanding of lesions and their spatial relationships. It also reveals changes in tumor morphology and tissue density determines the stage of PC and evaluates the degree of invasion. The Japanese Pancreatic society (JPS)Criteria guide PC staging, with Stage I having no vascular invasion and metastasis, Stage II having enveloped cancer cell infiltration, Stage III having lymphatic metastasis, and Stage IV having distant lymph node metastasis [14].

Endoscopic Ultrasonography

EUS-guided tissue specimens (EUS-TS) and endoscopic retrograde cholangiopancreatography guided tissue specimens (ERCP-TS) are superior methods for diagnosing pancreatic disease, particularly PC, with a sensitivity of 98% and 86%, respectively, in a retrospective study [15].

Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) technology has significantly improved the accuracy and surgical resectability of pancreatic cancer (PC). MRI staging is consistent with surgical staging, with a sensitivity of 1.00 and specificity of 0.67. Differential diffusion-weighted imaging (DWI) plays a significant role in distinguishing PC from mass formation, making it more clinically meaningful than MDCT in preoperative staging and resectability assessment [16].

Endoscopic Retrograde Cholangiopancreatography

Endoscopic retrograde cholangiopancreatography (ERCP) diagnoses pancreatic head cancer by allowing cytopathological examination at the trans-nipple bile duct stent. It improves diagnostic accuracy in exogenous bile duct strictures and allows biopsy from the tumor ampulla. Probe-based confocal laser endoscopes show high sensitivity [17].

Treatment

Traditional PC treatment includes surgery, chemotherapy, radiotherapy, and palliative care. Recent research explores targeted therapy, immunotherapy, and microbial therapy, potentially combining with traditional methods.

Surgery

Surgical Resection Indication

Surgical treatment is the sole cure for PC, extending survival, and can be divided into resectable, handover, unresectable, or combined with distant metastasis [18].

Surgical Techniques

PC resection, including total and distal pancreatectomy, is used for early-onset PC, but only 10% of patients are diagnosed. About 60% have metastatic disease or poor performance. Laparoscopic surgery has been performed in large hospitals but is more demanding for doctors. Postoperative mortality risk has dropped to 3%, but the risk of postoperative prevalence remains high. Surgical indications have expanded from resectable to locally advanced disease, but resection remains the basic treatment for PC patients [19].

Chemotherapy

Chemotherapy is crucial for treating prostate cancer, with adjuvant chemotherapy significantly improving disease-free survival and overall survival. The FOLFIRINOX regimen, gemcitabine, and NAB-paclitaxel are preferred for metastatic patients. For locally advanced patients, combination therapy with chemotherapy and radiation therapy is preferred. Researchers are exploring other topical therapies, and neoadjuvant therapy combined with chemotherapy and surgical treatment is the only option for advanced unresectable cancer [20].

Radiotherapy

Radiation therapy uses X-rays to destroy or damage cancer cells, mainly used in patients with advanced pancreatic cancer. It is not better than chemotherapy and does not improve patient survival. There are four main forms: external beam radiation therapy, brachytherapy, which is used for internal radiotherapy, and external beam radiation therapy [21].

Targeted Therapy

Targeted therapy is successful in various cancer types, but pembrolizumab has been recently approved as a targeted treatment for metastatic prostate cancer (PDAC). However, other targeted drugs have failed in PC patients. A clinical study of 19 patients showed that a molecularly tailored treatment regimen reduced tumor markers by >50%, but 88% died within 3 months. New targets for targeted therapy include PEGPH20 and CKAP4[22].

Immunotherapy

Various cancers, such as melanoma, lung cancer, renal cell carcinoma, and head and neck squamous cell carcinoma, now have approval for immunotherapy. The immunosuppressive environment of Pancreatic Cancer makes it less immunogenic. Immunotherapy is not currently approved for PC patients. Immunotherapy has been used to test different treatments, such as chemotherapy, chemotherapy-radiotherapy, vaccines, and cytokine antagonism. However, some tumors develop resistance and relapse during ICB treatment. A study in the US found that interferon (IFNs) can be a double-edged sword in the tumor immune response. [23].

Microbial Therapy

Human microbiota plays a crucial role in cancer development and treatment response. Intestinal bacterial extracts pancreatic cancer (PC)hosts can prevent the activation of CD4+ and CD8+ T cells, causing higher activation of pattern recognition receptors in tumor macrophages. However, the mechanism

remains unclear, and the role of microbial-derived metabolites and microbial-matrix interactions in metastatic disease remains unclear. Human microbes and gut bacteria are important components of the Pancreatic Cancer tumor microenvironment, and microbial conditioning, such as fecal transplantation, is a strong candidate for future clinical trials [24].

Fluorouracil single therapy

Since the 1950s, 5-fluorouracil-based chemotherapy has been a major pancreatic cancer treatment regimen. Despite improved effects from combinations like Adriamycin, mitomycin C, cyclophosphamide, methotrexate vincristine, and cisplatin.

Necessity of MDT

Pancreatic cancer treatment in China involves various clinical fields, including surgery, gastroenterology, oncology, radiotherapy, pathology, medical imaging, and nuclear medicine. MDT (Multidisciplinary Decision-Treatment) model combines various departments to achieve the best therapeutic effect. The National Comprehensive Cancer Network (NCCN) guidelines and the Chinese Medical Association incorporate MDT into patient treatment, involving medicine, technology, nursing, and other disciplines [25]. This multidisciplinary approach improves treatment levels, reduces overtreatment, and improves patient survival and quality of life [Fig4]

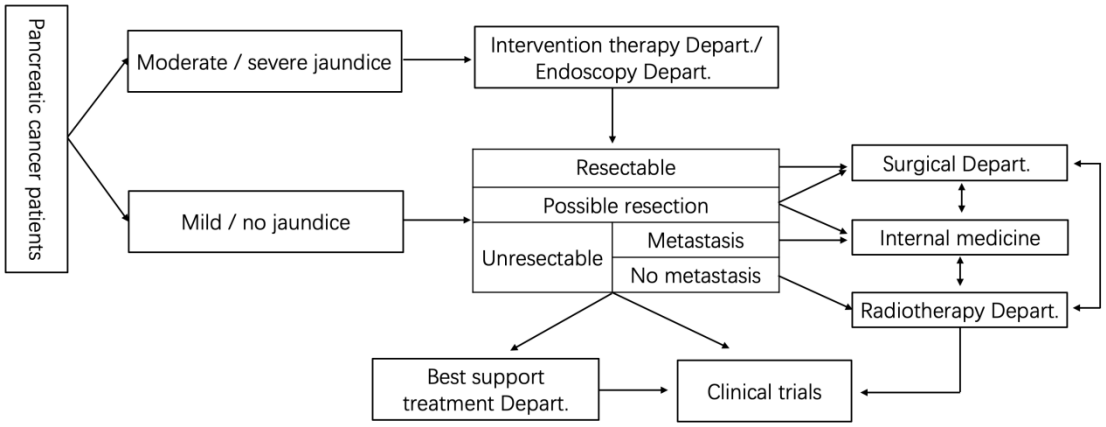

Fig 4 The path map of the MDT model in Pancreatic Cancer (version 1.2019)

The current landscape of MDT

Currently, many doctors in the Medical Oncology Treatment Team (MDT) lack awareness of multidisciplinary diagnosis and treatment for pancreatic cancer due to limitations in the existing medical system and different treatment methods from different disciplines. MDT forums help discuss difficult cases, improve diagnosis and treatment, and formulate personalized treatment plans. However, some doctors cannot participate due to reasons affecting the implementation of MDT. Nutritionists and psychiatrists cannot play a significant role in patient treatment, affecting MDT's benefits. MDT promotes communication between domestic and foreign counterparts, but there is insufficient communication at home and abroad. Young doctors rarely participate in MDT due to busy work and other reasons [26].

Future Prospects of MDT

The implementation of Medical Decision Tree (MDT) in pancreatic cancer diagnosis and treatment requires a distribution mechanism to protect doctors' income and rights, ensuring continuous operation.

MDT integrates resources from various disciplines and seeks individualized treatment for patients. However, progress in science and technology is needed to improve early diagnosis. The Internet + MDT (e MDT) model, combining MDT with the Internet, 5G, AI, and big data, can help improve patient care. This model can integrate remote consultation, joint outpatient services, and telemedicine, facilitating consultations between different medical institutions [27].

Palliative Care

Palliative care is crucial for PC patients, and three main management approaches include percutaneous bile duct drainage, surgical gastrojejunostomy, and endoscopic duodenal stents [28].

Future Treatment Directions for Pancreas Cancer

Current PC treatment strategies are limited, necessitating new therapeutic approaches, clinical studies, oncolytic virus therapy, microbial-chemotherapy combination, immunotherapy, and gene editing techniques [29].

Epidemiologic trends

China's pancreatic cancer incidence and mortality have significantly increased over the past two decades, compared to the global level. Despite being lower than the global level (6.57/100,000), the rate of increase has been much faster, reaching 4.33% in 2019. China's pancreatic cancer cases are increasing due to improved diagnostic technology and the aging population. Risk factors include unhealthy living habits and Helicobacter pylori infection. Folic acid is a protective factor [30]. It is advised to monitor the body's folic acid levels and consider taking folic acid supplements when they are low. The population ages, leading to increased deaths from pancreatic cancer due to poor diagnostic and treatment methods, resulting in a high recurrence rate and poor prognosis [31]. Chinese men have significantly higher smoking and drinking rates than women, with smoking being the most common risk factor for pancreatic cancer. A meta-analysis study found that smoking increases the risk of pancreatic cancer by 1.74 times compared to non-smokers. Long-term alcohol consumption, particularly in heavy drinkers, has also been associated with an increased risk of pancreatic cancer in men [32]. Our study reveals a significant increase in the disease burden of pancreatic cancer in China over the past 30 years, particularly in the population aged 70 and above. At present, we still know very little about the etiology of Pancreatic cancer and researchers need further large-scale prospective research to understand better the risk factors, new methods, and diagnosis and treatment related to PC, our study showed the incidence of pancreatic cancer is more common in the older age(>55 years old) and lower in 15-49 age group, The crude morbidity and mortality rates of pancreatic cancer were consistent, with higher rates in men and urban areas. The overall age-standardized morbidity rate increased by 2.78% annually, while the mortality rate increased by 2.24% annually [33]. The age effect on morbidity and mortality was most noticeable in the 70-80 age group. The crude incidence of pancreatic cancer is increasing worldwide, with women experiencing higher rates than men. This trend is slightly different in China, with higher human development indexes indicating a higher incidence and mortality rate of pancreatic cancer. Pancreatic cancer treatment in China has improved, but early diagnosis and motivation issues lead to a higher proportion of early and medium-term resection patients. Age is a risk factor for pancreatic cancer, with the highest incidence and death rates around 70-80 years old. Most of the pancreatic cancer patients are aged 50-80, with elderly patients having a significantly higher risk of developing the disease compared to young individuals [34]. In summary, the elderly have a high risk of disease and a poor prognosis, and the cohort effect of young people also rebounds, which suggests that we should still pay attention to the prevention and treatment of pancreatic cancer. There are limitations to this study. First, this study uses the public data from the China Cancer Report published in 2018–2023 for analysis. The original data comes from the international databases, which were mentioned above. There are some restrictions on the representation and extrapolation of results for the overall Chinese population.

Conclusion

Pancreatic cancer is a significant issue in China, particularly among the key population of older people, necessitating urgent attention and effective prevention strategies. The current understanding of PC etiology is limited, necessitating further prospective research to comprehend risk factors, new diagnosis methods, and treatment approaches. Screening for high-risk individuals, including familial PC families, can identify early-stage PC patients and increase their life span. However, the best screening age, time interval, and imaging techniques remain undetermined. The human microbial system may regulate tumor sensitivity to therapeutic drugs, improving PC treatment. Combining microbial systems with chemotherapy and immunotherapy could bring hope. Factors like smoking, obesity, and dietary intake also influence PC cell development. Understanding the microbial system is crucial for understanding PC occurrence and development. The microbial system can improve treatment effectiveness by monitoring changes in the microbiome during pancreatic cancer progression. Immunogenomics and gut microgenomics could lead to breakthroughs in the relationship between microbial systems and immunotherapy, potentially improving patient survival. However, immunotherapy for pancreatic cancer has faced challenges due to immune tolerance. Further research is needed to understand risk factors and develop new treatments.

Recommendations

Men over 40 who live in northeastern China must be closely monitored by medical professionals due to the high incidence of pancreatic cancer in this area. Early detection is crucial, as tumor markers are lacking. The resection and postoperative survival rates of advanced carcinoma are low. Comprehensive treatment is recommended for advanced carcinoma patients.

References

[1] Betriu N, Bertran-Mas J, Andreeva A, Semino CE. Syndecans and Pancreatic Ductal Adenocarcinoma. Biomolecules. 2021 Feb 25;11(3):349https://doi.org/10.3390%2Fbiom11030349

[2] Murage P, Bachmann MO, Crawford SM, McPhail S, Jones A. Geographical access to GPs and modes of cancer diagnosis in England: a cross-sectional study. Fam Pract.https://doi.org/10.1093/fampra/cmy077

[3] Y. Zhang, J. Yang, X. Cui, Y. Chen, V.F. Zhu, J.P. Hagan, H. Wang, X. Yu, S.E. Hodges, J. Fang, P.J. Chiao, C.D. Logsdon, W.E. Fisher, F.C. Brunicardi, C. Chen, Q. Yao, M.E. Fernandez-Zapico, M. Li, A novel epigenetic CREB-miR-373 axis mediates ZIP4-induced pancreatic cancer growth, EMBO Mol. Med. 5 (2013) 1322–1334.

[4] McMenamin UC, McCain S, Kunzmann AT. Do smoking and alcohol behaviours influence GI cancer survival? Best Pract Res Clin Gastroenterol. 2017;31(5):569-577.https://doi.org/10.1016/j.bpg.2017.09.015

[5] Jang YC, Leung CY, Huang HL. Association of Menopausal Hormone Therapy with Risk of Pancreatic Cancer: A Systematic Review and Meta-analysis of Cohort Studies. Cancer Epidemiol Biomarkers Prev. 2023 Jan 9;32(1):114-122. https://doi.org/10.1158/1055-9965.

[6] Jemal A, Siegel R, Xu J, Ward E. Cancer statistics, 2010. CA Cancer J Clin 2010; 60:277–300. https://doi.org/10.3322/caac.20073

[7] Li BQ, Wang L, Li J, Zhou L, Zhang TP, Guo JC, Zhao YP. Surgeons' knowledge regarding the diagnosis and management of pancreatic cancer in China: a cross-sectional study. BMC Health Serv Res. 2017 Jun 9;17(1):395. https://doi.org/10.1186/s12913-017-2345-6

[8] Wolfgang CL, Herman JM, Laheru DA, Klein AP, Erdek MA, Fishman EK, Hruban RH. Recent progress in pancreatic cancer. CA Cancer J Clin 2013; 63:318–348. https://doi.org/10.3322/caac.21190

[9] Chu D, Kohlmann W, Adler DG. Identification and screening of individuals at increased risk for pancreatic cancer with emphasis on known environmental and genetic factors and hereditary syndromes. JOP 2010; 11: 203-212.
[10] Ge L, Pan B, Song F, et al. Comparing the diagnostic accuracy of five common tumor biomarkers and CA19-9 for pancreatic cancer: a protocol for a network meta-analysis of diagnostic test accuracy. BMJ Open. 2017;7(12):e018175. https://doi.org/10.1136/bmjopen-2017-018175
[11] Goonetilleke KS, Siriwardena AK. Systematic review of carbohydrate antigen (CA 19-9) as a biochemical marker in the diagnosis of pancreatic cancer. Eur J Surg Oncol. 2007;33(3):266-270. https://doi.org/10.1016/j.ejso.2006.10.004
[12] Hufnagl C, Leisch M, Weiss L, et al. Evaluation of circulating cell-free DNA as a molecular monitoring tool in patients with metastatic cancer. Oncol Lett. 2020;19(2):1551–1558. https://doi.org/10.3892/ol.2019.11192
[13] He P, Yang JW, Yang VW, Bialkowska AB. Kruppel-like factor 5, increased in pancreatic ductal adenocarcinoma, promotes proliferation, acinar-to-Ductal metaplasia, pancreatic intraepithelial neoplasia, and tumor growth in mice. Gastroenterology (2018) 154(5):1494–508.e13. doi: 10.1053/j.gastro.2017.12.005
[14] Ghaneh P, Hanson R, Titman A, et al. PET-PANC: multicenter prospective diagnostic accuracy and health economic analysis study of the impact of combined modality 18fluorine-2-fluoro-2-deoxy-d-glucose positron emission tomography with computed tomography scanning in the diagnosis and management of pancreatic cancer. Health Technol Assess. 2018;22(7):1–114. https://doi.org/10.3310/hta22070
[15] Yeo SJ, Cho CM, Jung MK, Seo AN, Bae HI. Comparison of the diagnostic performances of same-session endoscopic ultrasound- and endoscopic retrograde cholangiopancreatography-guided tissue sampling for suspected biliary strictures at different primary tumor sites. Korean J Gastroenterol. 2019;73(4):213–218. https://doi.org/10.4166/kjg.2019.73.4.213
[16]Kamisawa T, Wood LD, Itoi T, Takaori K. Pancreatic cancer. Lancet 2016;388(10039):73–85. https://doi.org/10.1016/s0140-6736(16)00141-0
[17] Mikata R, Ishihara T, Tada M, et al. Clinical usefulness of repeated pancreatic juice cytology via endoscopic naso-pancreatic drainage tube in patients with pancreatic cancer. J Gastroenterol. 2013;48(7):866–873. doi:10.1007/s00535-012-0684-y
[18] Kamisawa T, Wood LD, Itoi T, Takaori K. Pancreatic cancer. Lancet 2016;388(10039):73–85. doi:10.1016/s0140-6736(16)00141-0.
[19] Strobel O, Neoptolemos J, Jager D, Buchler MW. Optimizing the outcomes of pancreatic cancer surgery. Nat Rev Clin Oncol. 2019;16(1):11–26. doi:10.1038/s41571-018-0112 -1
[20] Springfeld C, Jäger D, Büchler MW, Strobel O, Hackert T, Palmer DH, Neoptolemos JP. Chemotherapy for pancreatic cancer. Presse Med. 2019;48(3 Pt 2): e159–e174.doi: 10.1016/j.lpm.2019.02.025
[21] Chin V, Nagrial A, Sjoquist K, O'Connor CA, Chantrill L, Biankin AV, Scholten RJ, Yip D. Chemotherapy and radiotherapy for advanced pancreatic cancer. Cochrane Database Syst Rev 2018;3(3):CD011044. doi: 10.1002/14651858.CD011044.pub2
[22] Kimura H, Yamamoto H, Harada T, Fumoto K, Osugi Y, Sada R, et al. CKAP4, a DKK1 Receptor, Is a Biomarker in Exosomes Derived from Pancreatic Cancer and a Molecular Target for Therapy. Clin Cancer Res. 2019;25(6):1936-1947. doi: 10.1158/1078-0432.CCR-18-2124
[23] Benci JL, Johnson LR, Choa R, Xu Y, Qiu J, Zhou Z, et al. Opposing functions of interferon coordinate adaptive and innate immune responses to cancer immune checkpoint blockade. Cell. 2019;178(4):933–948. e914. https://doi.org/10.1016/j.cell.2019.07.019
[24] Schulz MD, Atay C, Heringer J, Romrig FK, Schwitalla S, Aydin B, et al. High-fat-diet-mediated dysbiosis promotes intestinal carcinogenesis independently of obesity. Nature 2014;514(7523):508–512. https://doi.org/10.1038/nature13398

[25] Oncologist Branch of Chinese Medical Association; Expert Committee on Pancreatic Diseases of China Association for the Promotion of International Health Care Exchange; Abdominal Cancer Expert Committee of China Medical Education Association. [Expert consensus on the MDT model of pancreatic cancer in China (2020 Edition)]. Zhonghua Zhong Liu Za Zhi. 2020 Jul 23;42(7):531-536. Chinese. doi: 10.3760/cma.j.cn112152-20200310-00192.
[26] Kirkegard J, Aahlin EK, Al-Saiddi M, Bratlie SO, Coolsen M, de Haas RJ, et al. Multicentre study of multidisciplinary team assessment of pancreatic cancer resectability and treatment allocation. Br J Surg (2019) 106(6):756–64. doi: 10.1002/bjs.11093
[27] Dulai R, Shunmugam SR, Veasey RA, Patel NR, Sugihara C, Furniss S. An economic evaluation of an advanced video conferencing system for cardiac multidisciplinary team meetings. Int J Clin Pract (2020) 74(9):e13562. doi: 10.1111/ijcp.13562
[28] Kamisawa T, Wood LD, Itoi T, Takaori K. Pancreatic cancer. Lancet. 2016;388(10039):73–85. doi:10.1016/s0140-6736(16)00141-0.
[29] McGuigan A, Kelly P, Turkington RC, Jones C, Coleman HG, McCain RS. Pancreatic cancer: a review of clinical diagnosis, epidemiology, treatment and outcomes. World J Gastroenterol. 2018;24(43):4846–4861. https://doi.org/10.3748/wjg.v24.i43.4846
[30] Wu WR, He XK, Yang LY, Wang Q, Bian XY, Ye JZ, et al. Rising trends in pancreatic cancer incidence and mortality in 2000-2014. Clin Epidemiol 2018;10:789 – 97.
[31] Salman B, Zhou DE, Jaffee EM, Edil BH, Zheng L. Vaccine therapy for pancreatic cancer. Oncoimmunology 2013;2(12):e26662.
[32] Iodice S, Gandini S, Maisonneuve P, Lowenfels AB. Tobacco and the risk of pancreatic cancer: a review and meta-analysis. Langenbeck's Arch Surg 2008;393(4):535 − 45
[33] Cai J, Chen HD, Lu M, Zhang YH, Lu B, You L, et al. Trend analysis on morbidity and mortality of pancreatic cancer in China, 2005-2015. Chin J Epidemiol 2021;42(5):794 − 800