Cancer Screening and Prevention **2024** vol. 3(3) | 154–162
DOI: 10.14218/CSP.2024.00006

Review Article

Advances in Screening and Early Diagnosis of Pancreatic Cancer

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Received: August 13, 2024 | **Revised:** August 31, 2024 | **Accepted:** September 19, 2024 | **Published online:** September 25, 2024

Abstract

Pancreatic cancer (PC) remains a formidable challenge in oncology due to its notoriously poor prognosis, often resulting from late-stage diagnosis. Early detection through effective screening methods is crucial not only to improving patient outcomes but also to enhancing their quality of life. This review focuses on the latest advancements in PC screening and early diagnostic strategies. Key areas include the integration of artificial intelligence in radiology, the search for novel biomarkers, and the development of predictive models. This review aimed to provide a comprehensive overview, serving as a stepping stone toward transforming early detection strategies for PC in the digital age.

Introduction

Aggressive progression and insidious symptoms often result in pancreatic cancer (PC) patients receiving diagnoses at late stages. Therefore, treatment landscapes and survival rates have remained pessimistic, even with advancements in oncology. According to Cancer Statistics 2024, PC ranked 4th among the leading causes of cancer death across all age groups in the United States, with an estimated 66,440 new cases and 51,750 deaths reported in 2024.[1] In China, 118,672 new PC cases were reported in 2022, with an incidence rate of 4.4 per 100 and a mortality rate of 3.9 per 100. In contrast, global statistics reported 510,992 new cases, an incidence rate of 4.7 per 100, and a mortality rate of 4.2 per 100.[2]

Ethnically, the Asian population may be more susceptible to PC in the presence of certain disease backgrounds, such as gallstones and Crohn's disease.[3,4] Additionally, the large number of PC patients and deaths in China has created significant medical and socioeconomic burdens, warranting immediate attention. PC patients require a considerable amount of healthcare resources, leading to a substantial number of hospitalizations and medical costs significantly higher than those for other cancer types.[5] The rising incidence and associated costs have contributed to PC's growing burden, especially in regions with rapid economic growth and aging populations, such as China.[6,7] PC's 5-year overall survival rate is currently 13%.[1] Early diagnosis, however, holds great promise for improving patient outcomes, overall survival rates, and associated costs. Studies have shown that patients diagnosed at an early stage exhibit significantly improved survival outcomes, with a median overall survival of nearly 10 years compared to 1.5 years for those diagnosed at later stages.[8] Consequently, it is imminent to implement prevention strategies and early detection programs to screen this disease early.[7]

The challenge of conducting effective early screening for PC stems from three main factors: 1. The lack of indicative risk factors; 2. the absence of reliable, specific, and sensitive screening protocols; and 3. the relatively low prevalence of PC in the general population. The mechanisms behind PC incidence and progression remain poorly understood,[9] hindering the identification of serum biomarkers strongly associated with early disease onset. While the development of endoscopic ultrasonography (EUS) and endoscopic retrograde cholangiopancreatography has improved sensitivity and specificity in PC screening, issues such as a shortage of trained operators and long appointment wait times have failed to meet clinical needs.[10] Furthermore, the low sensitivity and laborious protocols of current detection methods present significant obstacles to large-scale screening efforts.[11] Although serum biomarker carbohydrate antigen 19-9 (CA19-9) is routinely used in clinics to diagnose PC, its limited sensitivity and specificity undermine its

Keywords: Early diagnosis; Pancreatic cancer; Early screening; Novel strategies; Non-invasive diagnostic methods; Liquid biopsy; Radiomics in pancreatic cancer; Artificial intelligence in cancer detection.

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How to cite this article: Luo W, Wang J, Chen H, Cao Z, Qiu J, Liu Y, *et al*. Advances in Screening and Early Diagnosis of Pancreatic Cancer. *Cancer Screen Prev* 2024;3(3):154–162. doi: 10.14218/CSP.2024.00006.

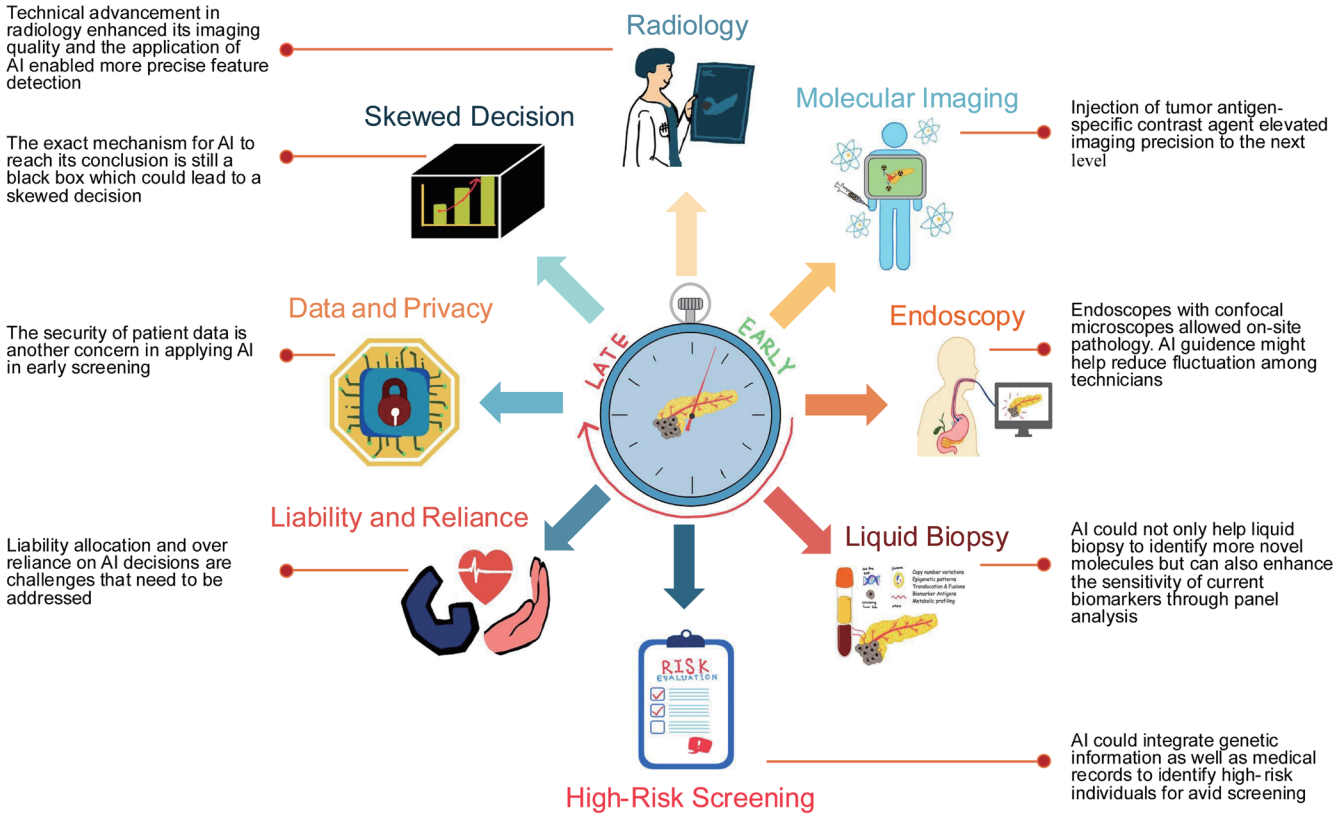

Fig. 1. An illustration of integrating artificial intelligence in various regimes to aid in identifying pancreatic cancer promptly. AI, artificial intelligence.

reliability in early detection despite widespread use.[12] Finally, the relatively low prevalence of PC makes extensive screening infeasible.[9] Therefore, further research into imaging techniques, early-stage biomarkers, and predictive risk factors is imperative for developing timely, specific, convenient, and cost-effective screening methods.

This review will discuss the latest advancements in early PC detection, including radiology, serum markers, and the incorporation of artificial intelligence (AI). By critically evaluating the strengths and limitations of existing technologies, this study endeavored to elucidate optimal strategies for early detection protocol development for scientists, engineers, and physicians (Fig. 1).

Advancements in diagnostic technologies

Significant strides have been made in radiology for screening pancreatic lesions in recent years. High-resolution computed tomography (CT), magnetic resonance imaging (MRI) with diffusion-weighted sequences, and EUS have emerged as front-line tools for identifying pancreatic lesions at early stages, when curative interventions may still be viable. EUS, particularly contrast-enhanced EUS, has enabled efficient imaging, differential diagnosis, and staging of pancreatic lesions that might otherwise be missed by other imaging modalities.[13,14] Concurrently, advancements in more sensitive molecular detection methods have rapidly expanded biomarker research, leading to the identification of reliable hematological indicators for early PC screening. Liquid biopsy, a non-invasive technique, can detect various biomarkers, from circulating tumor cells to tumor RNA, in blood, urine, and pancreatic juice.[15] As more novel biomarkers, including proteins, genetic signatures, DNA, RNA, and exosomes, are identified through liquid biopsy,[15] integrated data may help reveal the mechanisms of cancer development. Beyond screening, the application of liquid biopsy extends to monitoring treatment response, evaluating prognosis, and identifying therapeutic targets.[15]

In addition to developing more precise imaging and sampling methods, the integration of AI into nearly every aspect of early diagnostic tools has been unprecedented and indispensable. AI-driven approaches show promise in streamlining the diagnostic process. By synthesizing diverse sources of information from radiology, serum biomarker panels, health records, etc., AI programs can potentially identify high-risk individuals and early-stage pancreatic lesions with much greater accuracy than human capabilities.[8,16] Undoubtedly, the incorporation of AI will enhance the efficiency and precision of medical professionals' work. However, various concerns accompany these advancements, requiring comprehensive solutions to address biases, transparency, privacy, liability, and ethical considerations.[17]

CT, positron emission tomography (PET)-CT, & MRI

Diffusion-weighted imaging (DWI) and contrast were used to further enhance MRI scan details. By analyzing water molecules, DWI MRI can reveal tissue microstructures, enabling differentiation between healthy and pathological regions with increased sensitivity.[18] MRI with DWI significantly improves diagnostic accuracy and the detection of early-stage cancer.[19] Through the use of contrast agent injections, dynamic contrast-enhanced MRI (DCE-MRI) allows for both qualitative and quantitative assessments of

tumor lesions. Although quantitative DCE-MRI is currently limited to clinical trials, ongoing efforts are proposing standardized protocols for recruiting DCE-MRI to clinical practice.[20]

Fibroblast activation protein (FAP), predominantly found in activated fibroblasts associated with cancer, chronic inflammation, and fibrosis, is a type II transmembrane protease with both dipeptidyl peptidase and endopeptidase activities. FAP is involved in tissue remodeling, angiogenesis, and collagen degradation. The FAP inhibitor (FAPI) is a radiolabeled quinoline tracer designed for PET.[21] Specifically, [68Ga]Ga-FAPI-04 PET has demonstrated high expression in various cancers, including those with low [18F]-FDG affinity, and minimal uptake in most healthy tissues. Recent studies of [68Ga]Ga-FAPI-04 PET suggest its potential to predict tumor invasiveness, provide prognostic information, and assist in treatment decision-making.[22,23]

The increasing detail in medical imaging introduces an overwhelming amount of information, often indecipherable to the human eye, providing an opportunity for AI to excel. AI applications in medical imaging have ushered in a new era of early PC diagnosis, where robust feature detection and subtle pattern recognition are now possible. Machine learning and deep learning algorithms are particularly adept at analyzing complex imaging datasets from medical scans, including CT, MRI, and PET scans, giving rise to the new field of "radiomics".[24,25] These algorithms can detect subtle changes in pancreatic morphology and identify small, potentially malignant lesions that may escape traditional radiological interpretation, allowing clinicians to detect pancreatic abnormalities at an earlier and potentially more treatable stage. By training algorithms with CT or MRI scans labeled with PC lesions, they have shown higher sensitivity for PC diagnosis compared to radiologists.[26] Deep learning and radiomics not only enhance the accuracy and efficiency of PC diagnosis but also demonstrate a high level of generalizability, accommodating individuals from various ethnic backgrounds (The performance of AI models was evaluated using several key measures. The models achieved a mean accuracy of 89.4%, ranging from 71.6% to 99%. The area under the curve had a mean value of 88.05%, ranging from 86% to 95.3%. Precision averaged 69.1%, ranging from 14% to 99.5%. Sensitivity was high, with a mean of 91.3%, ranging from 60% to 99.9%, while specificity averaged 83.2%, with a range of 69.5% to 100%. These results indicate strong overall performance across different metrics).[16,26] Li *et al*.[27] also developed a novel causality-driven graph neural network to analyze CT scans. This innovative learning algorithm yielded promising results in enhancing the stability and generalization of early PC diagnosis and may serve as a valuable clinical tool in the foreseeable future. AI technologies undoubtedly hold great promise in developing automated systems to identify subtle features indicative of early-stage PC. While there is still a long way to go before AI technologies can function independently in medical diagnosis, they could significantly aid physicians in improving early detection rates and patient outcomes.[28]

In summary, enhanced visualization and AI integration in medical imaging have significantly improved the accuracy and efficiency of early detection, precise staging, and treatment planning for PC.

Molecular imaging

In addition to detecting PC early by analyzing image features, Zhu *et al*.[29] developed a nanoplatform to deliver MRI contrast agents with cancer specificity. These peptide-functionalized polymeric magnetic nanoparticles were selectively internalized by PC cells through specific bonding. This differential binding created a contrast enhancement between healthy and cancerous pancreatic tissue and holds promise for targeted imaging in the early diagnosis of PC.[29] A similar approach, where molecular-level targets were selected to enable specific and sensitive imaging, was applied in functional imaging techniques, including single-photon emission computed tomography and PET. Wang *et al*.[30] used a radioactively labeled inhibitor to integrin α5 (ITGA5), a protein specifically overexpressed in the pancreatic stroma, to enhance single-photon emission computed tomography/CT scans of PC in a mouse xenograft model. Though a preliminary study, this method offered valuable insights into how advances in imaging specificity and treatment specificity could complement each other.

AI also played a role in accelerating biomarker recognition that could be employed in molecular imaging. Combining AI with hyperpolarized magnetic resonance and multimodal imaging data facilitated the discovery of real-time biomarkers to detect PC early.[31] This fusion of AI with advanced imaging technologies holds great promise for transforming the early detection and management of PC.

Endoscopic ultrasonography

Challenges exist when applying EUS to the early detection of PC. Many different types of pancreatic lesions present with a similar hypoechoic appearance on EUS, making it difficult to differentiate between benign and malignant lesions based solely on images.[32] Moreover, for pancreatic tumors around 2–3 cm, EUS can achieve satisfying sensitivity compared to other radiological images, but this sensitivity drops rapidly as lesion size decreases.[33] It is especially challenging to widely adopt EUS for early diagnosis when lesions are usually minimal. Though EUS images alone sometimes fail to provide the sensitivity and accuracy desired for early PC diagnosis, its visual guidance is undoubtedly valuable and has led to advancements in operations, from biopsy of pancreatic tissue to treatment and symptom relief.[34]

The application of AI in EUS-related operations is also noteworthy. AI algorithms, incorporating artificial neural networks and region-based convolutional neural networks, have been used for early and precise PC identification. AI and endoscopists can help verify each other's judgments to avoid missed readings.[35] In a meta-analysis by Yin *et al*.,[36] AI-assisted image classification demonstrated an accuracy of 0.95 in PC prediction, a sensitivity of 93%, and a specificity of 90%. This high level of accuracy likely stems from AI's unbiased nature in reading image details, reducing the intrinsic variability among EUS operators.[37] Operating and interpreting EUS results require years of specialized training. Unequal distribution of EUS specialists can result in healthcare disparities, making certain populations more susceptible to missed early PC diagnoses. Certain AI algorithms have achieved specimen recognition levels comparable to EUS experts,[38] which could be crucial in reducing disparities in timely PC diagnosis due to a lack of specialists.

In conclusion, EUS and its associated procedures are foundational to the early diagnosis of pancreatic cancer, given their high diagnostic accuracy, safety, and versatility in obtaining tissue samples for cytological and histological assessments. AI image classification offers great support to endoscopists by providing additional security checks and could potentially reduce disparities in early PC diagnosis. Moreover, live AI-assisted EUS operations or training programs could help improve PC patient outcomes by reducing variability between skilled and less experienced EUS technicians.

Liquid biopsy

Exosomes are a significant liquid biopsy approach for the early diagnosis of PC due to their minimal invasiveness.[39] Research by Yu

et al.[39] developed a nanoliquid biopsy test to enhance PC exosome detection while addressing low specificity and sensitivity, labor-intensiveness, and technical obstacles. Liquid biopsy of cell-free DNA has also demonstrated its potential as an adjunct to standard care for PC patients.[40]

Piwi-interacting RNAs, which act as epigenetic modulators, were identified from pancreatic tissue through liquid biopsy to differentiate healthy individuals from PC patients. Additionally, the detection of Piwi-interacting RNAs enhanced the diagnostic potential of the serum marker CA19-9 for early PC detection.[41]

However, the effectiveness of liquid biopsies for early cancer detection varies greatly depending on the technique and tumor type. To improve performance, intensive inspections of the circulome and comprehensive profiling of a panel of biomarkers, including circulating tumor cells (CTCs), circulating tumor DNA (ctDNA), extracellular vesicles, etc., could be applied, although the diagnostic validity and accuracy warrant further investigation.[42]

Liquid biopsy holds the potential to facilitate a prompt, minimally invasive, and accurate diagnosis of PC. As more molecules are discovered through liquid biopsy, understanding the genesis and progression of cancer will improve, expediting early PC detection.

Traditional serum markers

CA19-9 and carcinoembryonic antigen are widely used serum markers in clinical practice to screen PC, despite their unsatisfactory specificity and sensitivity.[43] CA19-9, the sole biomarker authorized by the United States Food and Drug Administration, is more indicative of treatment response monitoring than early PC detection.[44] Panel analysis of different biomarkers in combination with CA19-9 has enhanced the accuracy of early PC detection. Xiao *et al*.[45] created a detection panel consisting of the exosomal surface protein glypican-1, an exosomal cluster of differentiation-82, and serum CA19-9. This panel exhibited excellent diagnostic accuracy (AUC = 0.942) in distinguishing healthy individuals, pancreatitis patients, and PC patients, holding the potential to become a standard PC screening protocol.[45] Suehiro *et al*.[46] also evaluated the diagnostic performance of serum-methylated Homeobox A1 and methylated somatostatin in combination with CA19-9 using the combined restriction digital PCR assay. The sensitivity for stage I PC increased from 50% during a single-marker test of CA19-9 to above 85% when other biomarkers were included in the diagnosis.[46] This multiplex approach shows promise in improving the specificity and sensitivity of early PC screening.

Ongoing research is focused on identifying novel biomarkers and adjusting multi-marker panels. The diagnostic cocktail of traditional markers combined with other macromolecules and metabolic profiling data will further enhance screening methods to detect PC at earlier stages.

Other serum markers

Metabolomic profiling involves the comprehensive analysis of small-molecule metabolites in biological samples. Altered metabolic pathways in PC cells can lead to distinct metabolite profiles in patient biofluids and therefore could serve as a gateway for early detection and disease monitoring. Research has delved into the role of metabolites and genetic signatures, such as single nucleotide polymorphisms, in predicting PC risk to enable early diagnosis and therapeutic interventions.[47] Serum fatty acid synthase levels are significantly elevated in PC patients and have been proposed as a diagnostic marker for early PC detection.[48] However, it is still unclear how early fatty acid synthase levels rise in the bloodstream, which complicates determining an appropriate timeline for early PC diagnosis. Elevated levels of serum ferritin are also indicative of PC and could be applied to identify at-risk individuals for early intervention.[49]

Furthermore, chronic inflammation markers, including C-reactive protein, albumin, haptoglobin, and leukocytes, are associated with the risk of PC. Analysis of these expression patterns could potentially be used to assess PC risk.[50] Another notable advancement in isolating serum markers for PC involves utilizing a microfluidic immunoassay system for the rapid detection and semi-quantitative determination of the potential serum biomarker mesothelin.[51]

CTCs

Many CTCs enter the bloodstream early in tumorigenesis through passive shedding from the primary tumor site.[52] Therefore, CTCs are theoretically suitable for early cancer screening. CTCs were identified and analyzed in PC alongside other macromolecules through liquid biopsy for detection and early disease screening.[11] Vimentin was used as an antigen to extract serum CTCs in PC patients, presenting satisfactory diagnostic potency alongside CA19-9.[53] CTCs isolated from preoperative blood draws could predict the early recurrence of PC, rendering them a valuable tool for monitoring disease progression.[54] In addition to serum, CTCs and ctDNA from pancreatic juice have also been recognized for their contributions to early PC diagnosis.[55]

As more biomolecules become available through liquid biopsy, CTCs are increasingly evaluated alongside other biomarkers to provide more accurate and comprehensive information regarding early tumor genesis and disease progression.

Exosomes

Primarily extracted through liquid biopsy, tumor exosomes (T-Exos) have emerged as essential components of the biomarker panel for early PC diagnosis. Yu *et al*.[39] developed a nano-liquid biopsy assay to detect PC T-Exos with excellent specificity, ultrahigh sensitivity, and cost-effectiveness. T-Exos can be detected at concentrations as low as 78 pg/mL.[39] Moreover, Li *et al*.[56] employed a hierarchical surface-enhanced Raman scattering substrate and a rapid enrichment strategy using magnetic beads to successfully enhance the quantitative detection of exosomes specific to PC, even at early stages.

Circulating nucleotides

ctDNA is fragmented tumor DNA released from tumor sites and shows promise as a tumor-specific biomarker for PC.[57] ctDNA serves as a non-invasive tool for early diagnosis, molecular characterization, and monitoring of tumor progression in PC. While preoperative ctDNA is a prognostic marker for poor survival, postoperative ctDNA levels indicate minimal residual disease. ctDNA also shares genetic information with the primary tumor site, thus aiding in directing personalized treatment.[58]

Two main approaches to identifying genetic alterations in ctDNA are advanced PCR-based techniques, which are highly sensitive in targeting known mutations, and NGS-based techniques, which can analyze multiple alterations in a single experiment, albeit with a sacrifice of sensitivity.[59–61] Evaluation of ctDNA through liquid biopsy presents a promising tool for early diagnosis and personalized treatment of PC.[62] A recent study by Bayle *et al*.[63] found that ctDNA genetic testing could enhance and potentially substitute tissue testing, based on data from over 1,000 enrolled patients. However, detecting ctDNA at lower concentrations

remains challenging.[58] Additionally, normal aging and the accumulation of blood cell mutations could contribute to false positives in ctDNA analysis.[64]

Circular RNAs also show promise as biomarkers for early diagnosis. hsa_circ_0013587, identified through qRT-PCR, is elevated in serum samples of PC patients. Though detected in the early stages of PC, the expression of hsa_circ_0013587 is more upregulated in PC patients at later stages.[65] Therefore, guidelines and more reliable testing techniques are needed to ensure the detection of hsa_circ_0013587 at lower levels for early diagnosis. Long non-coding RNAs are also being explored as potential biomarkers for PC diagnosis and prognosis prediction, as they are involved in various cellular functions.[66]

Integration of information by AI

As tumor cells are a dynamic biological entity, it is nearly impossible to determine the existence of cancer-based on a singular result. Therefore, integrated information from a panel of multiple biomarkers, including proteins, genetic mutations, and epigenetic alterations, is being developed to improve diagnostic accuracy. To manage the overwhelming amount of information, AI has become a valuable tool for searching and interpreting non-invasive biomarkers for the timely detection and intervention of PC.[67]

A deep learning model, Pancreatic Cancer Detection with Artificial Intelligence, demonstrated high accuracy in detecting and classifying pancreatic lesions using non-contrast CT scans. Trained on a dataset of 3,208 patients from a single center, this model achieved an AUC ranging from 0.986 to 0.996 in a multicenter validation involving 6,239 patients across ten centers. It outperformed the average radiologist's performance by 34.1% in sensitivity and 6.3% in specificity for identifying pancreatic ductal adenocarcinoma. In real-world scenarios, the model achieved a sensitivity of 92.9% and a specificity of 99.9% in detecting lesions among 20,530 consecutive patients. Notably, the model's performance with non-contrast CT was comparable to radiology reports using contrast-enhanced CT when distinguishing common pancreatic lesion subtypes. This accuracy instills confidence in applying the model as a valuable tool for large-scale PC screening.[68]

Moreover, mass spectrometry, machine learning, and liquid biopsy have facilitated the identification of clusters of biomarkers for PC diagnosis.[69] By amalgamating multiple biomarkers, researchers aimed to overcome the limitations of existing screening tools and enhance the overall management of PC.

AI has been instrumental in compiling imaging data, biomarker profiles, and clinical information to identify subtle abnormalities indicative of PC.[16] Machine learning algorithms have helped integrate diverse data sources to enhance patient care.

Screening and identifying high-risk individuals

From an epidemiological perspective, it is impossible to screen the general population for PC. Therefore, medical professionals in primary care or community medical facilities must identify high-risk individuals to conduct routine and targeted screening. Routine EUS and/or MRI/magnetic resonance cholangiopancreatography (MRCP) are recommended for screening high-risk individuals once they are identified.[70]

The development of PC is influenced by both genetic and environmental factors.[7] Genetic factors include familial PC, hereditary pancreatitis, known genetic mutations, and syndromes that render certain populations more susceptible.[71] A genome-wide association study found that variants in the ABO locus are associated with a differential risk of PC, with blood types A and B contributing to a higher risk compared to blood type O.[72] SIK3 has been identified as a potential new susceptibility gene predisposing its carriers to PC.[73] Germline pathogenic variants of genes, including *BRCA1/2*, *PALB2*, *ATM*, and *RAD17*, are linked to familial PC cases.[74,75] Variations at the single nucleotide level also exerted an effect on PC risk; eight single nucleotide polymorphisms associated with increased susceptibility have been identified on chromosomes 13q22.1, 1q32.1, and 5p15.33.[76]

Furthermore, epigenetic modifications can alter PC risks. Joris *et al*.[75] investigated methylome data and identified 45 cytosine-phosphate-guanine (CpG) sites associated with PC risk. These genetic variations and their regulation predispose individuals to PC and can influence familial aggregation patterns, highlighting the importance of genetic testing in high-risk populations.

In addition to genetic factors, lifestyle choices such as alcohol consumption and smoking, medical histories such as diabetes and chronic pancreatitis, and environmental exposures play intricate roles in PC risk.[7] Interactions between genetic predisposition and environmental factors influence this risk. Significant associations have been found between poor oral hygiene and NR5A2 rs2816938, as well as between obesity and PDX1 rs9581943, highlighting gene-environment interactions.[51]

Collectively, lifestyle factors, medical histories, genetic polymorphisms, and gene-environment interactions influence the elevated risk of PC. Therefore, it is essential to conduct a comprehensive analysis of these various components. AI and machine learning can enhance patient risk stratification by integrating a range of input factors, streamlining the identification of high-risk individuals.[77] Risk models based on clinical characteristics, genetic polymorphisms, and biomarkers improve precision in disease recognition compared to models that rely solely on clinical factors.[78] Placido *et al*.[79] constructed AI models to retrospectively analyze clinical data from millions of patients in Denmark and the United States, identifying critical trajectories indicative of PC. These models can significantly enhance surveillance programs for at-risk patients to detect PC early.[79]

A combination of genetic, epigenetic, and environmental factors influences PC risk. Understanding the genetic backgrounds that predispose individuals to PC is crucial for early detection and intervention. Until widely available genetic testing and screening become a reality, AI algorithms that analyze medical records and lifestyle choices hold substantial promise in identifying at-risk individuals from the general population for further examination.

Challenges and advantages in applying AI to clinical settings

AI is a valuable tool that significantly enhances the early diagnosis of PC from various perspectives. Algorithms can efficiently identify at-risk individuals by processing substantial amounts of information from medical images, pathological examinations, biomarkers, and other factors.[8] AI algorithms equip medical professionals with precise decision-making tools for early screening, diagnosis, and management of PC.[80] This increased accessibility to convenient screening approaches may also help alleviate disparities in medical services for disease management.

However, the application of AI in clinical practice is not without concerns. Potential biases intrinsic to AI algorithms can lead to skewed outcomes and decisions.[81] A lack of transparency regarding information safety and associated risks is another major concern. Significant gaps in documentation about AI training data and ethical considerations raise issues of trust and accountabili-

ty.[82] Privacy concerns, challenges to job security among healthcare professionals, and over-reliance on AI must all be carefully addressed.[83] Additionally, the reallocation of responsibility between AI and healthcare providers should be optimized to ensure maximum patient safety.[83]

The new era of AI has prompted many professional fields to address issues of data bias, transparency, privacy, liability, and ethical considerations in clinical settings. By actively acknowledging these concerns, the integration of AI in the early diagnosis of PC can be continuously optimized.

Future directions

Successful early diagnosis of an insidious malignancy such as PC requires a multifaceted approach. Current challenges primarily consist of a lack of highly specific and cost-effective markers indicative of early stages, alongside high screening costs due to the relatively low incidence among the general public. Therefore, future research efforts should focus on developing low-cost, efficient, early, and specific screening strategies.

Studies on molecular pathways involved in early tumorigenesis and progression, including CIRBP, p53, and RAD51, represent significant advancements in developing early diagnostic regimens.[84,85] A deeper understanding of molecular mechanisms will aid in identifying markers that emerge at increasingly earlier stages of cancer development. As previously mentioned, these markers could be utilized in molecular imaging to generate highly tumor-specific scans, enabling radiologists to detect subtle changes that might otherwise be overlooked.

The discovery of molecular biomarkers hinges on the development of accurate and economical cell assays. Liquid biopsy has ushered in a new era for detecting a broad range of molecules at various cancer stages. However, its high material costs and complex procedures remain significant barriers to widespread application in routine screening. With AI's assistance, the utility and efficiency of liquid biopsy could be significantly amplified. AI could help identify and analyze key targets in a panel of biomarkers, potentially simplifying the number of biomarkers needed in a single test.

The development and application of AI tools for PC screening based on imaging results and medical records may be more achievable than addressing other technical challenges that require a deeper understanding of physical and life sciences. Collaboration among AI developers, government officials, and medical professionals is essential to resolve ethical and liability concerns and facilitate the broad application of AI-assisted screening programs.

Last but not least, screening and advocacy efforts from clinicians to improve patient education represent the most cost-effective yet significant strategies. The impact of social determinants of health on PC diagnosis and survival has garnered attention, with studies suggesting that addressing modifiable social risk factors could enhance early diagnosis rates and ultimately improve patient outcomes.[86] Understanding the interplay between social determinants of health and disease prognosis is crucial for developing holistic approaches to PC management that extend beyond traditional medical interventions.

Future directions in early diagnosis of PC lie in the collaboration of innovative biomarker identification, the application of artificial intelligence tools, and the dedicated efforts of medical personnel. Continued interdisciplinary collaboration and translational research are essential to realizing these transformative potentials and addressing the challenges posed by this devastating disease.

Despite the variety of advanced technologies available for early diagnosis of PC, notable limitations persist. Current research on these technologies is often superficial and lacks in-depth validation. While promising diagnostic tools, such as advanced imaging techniques, biomarkers, and liquid biopsies, have been developed, their clinical translation and prospects for general adoption remain limited. The gap between theoretical advancements and practical implementation in clinical settings needs to be narrowed.

Although this article proposes a novel early diagnostic model based on AI, the supporting research for its clinical application is sparse. Relatively few studies explore how AI-based models perform in real-world clinical environments, limiting our understanding of their efficacy and integration into routine practice. Addressing these gaps through more comprehensive research and clinical trials is essential for advancing the field and improving early diagnosis strategies for PC.

Conclusions

PC screening and early diagnosis are rapidly evolving due to advancements in imaging technologies, biomarker discovery, and artificial intelligence. Despite challenges such as cost, accessibility, and ethical concerns, ongoing research holds promise for improving early detection rates and patient outcomes. Continued interdisciplinary collaboration and the integration of innovative technologies are essential to translate these advancements into effective clinical practice.

Acknowledgments

None.

Funding

This study was supported by grants from the National Natural Science Foundation of China (No. 82203158, No. 82103016, No. 82172836, No. 82272917, No. 62133006); CAMS Innovation Fund for Medical Sciences (CIFMS, 2021-I2M-1-002); the National Multidisciplinary Cooperative Diagnosis and Treatment Capacity Building Project for Major Diseases; the Beijing Natural Science Foundation (No. 7242104, No. 7244385); the Research and Translational Application of Clinical Characteristic Diagnosis and Treatment Techniques in the Capital (Z221100007422070); the Beijing Science and Technology Plan (Z231100007223006); the Postdoctoral Fellowship Program of CPSF under Grant Number GZB20240074; and the National High-Level Hospital Clinical Research Funding (2022-PUMCH-A-245).

Conflict of interest

One of the authors, Prof. Taiping Zhang, has been an associate editor of *Cancer Screening and Prevention* since March 2022. The authors have no other conflicts of interest.

Author contributions

Study design (WHL), literature search (JW), study draft and revision (WHL, JW, HC, ZC, JDQ, YZL, GY, JXT, LYY, GHW, TL, HH, JCX, XYL, CD, YFF, YYW, MGZ), and supervision (LY, TPZ). All authors have approved the final version and publication of the manuscript.

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